JUL 8 - 1932

VOLUME 25 NUMBER 1

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JULY, 1932

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, July 10, 1925, at the Postoffice at Chicago, Illinois, Under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of Oct. 3, 1917, authorized July 29, 1920.

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ARCHIVES OF SURGERY

VOLUME 25 JULY, 1932 NUMBER 1

CONGENITAL MALFORMATIONS OF THE HANDS

ALLEN B. KANAVEL, M.D.

CHICAGO

The difficulties that confront the physician when he attempts to correlate the various congenital deformities of the hand that he has observed are many and perplexing. Since the etiology of some types is still not established, a scientific classification cannot be made at the present time. It may be possible, however, to simplify the picture, coordinate the known facts and marshal the various descriptive terms into some semblance of order.

Lobster-claw hand, ectrodactylism, club hand, brachydactylism, gigantism, hypodactylism and other descriptive terms have a place in the classification, but as knowledge of the etiology and pathologic processes increases, other terms more definitely descriptive and more clarifying in their relation to other lesions should supplant them.

The material used for this statistical study consists of sixty private patients, studied in the hospital. The patients were on the common service of my associates, Dr. Sumner Koch and Dr. Michael Mason, and myself. A much larger group who were seen in consultation, and many of our own patients for whom we judged there was no operative indication have not been included since, as the patients had not been on our hospital service, adequate study and records are not available. A study of our patients and a survey of the literature demonstrate that in large measure the various lesions may be grouped into those showing: (*a*) hypoplasia and aplasia, (*b*) disorientation of tissue and (*c*) hyperplasia. It is also found that these various malformations have a predilection for certain parts of the hand and forearm; roughly speaking, they may be divided into radial and ulnar lesions which may involve either the ulna or radius and their radicles or both in varying degree. One may find, for instance, an absence of the ulna, a reduplication of the ulna with the radius practically normal, an absence of the radius, a fusion or absence of the radial or ulnar carpal bones, a lack of growth of the ulnar or of the radial elements (brachydactylism, brachyphalangism and ectrodactylism), a reduplication of radial or ulnar digits (polydactylism) or a syndactylism of the digits, etc. The mal-

From the Surgical Department of Northwestern University Medical School.

Chairman's address, read before the Section on Surgery, General and Abdominal, at the Eighty-Second Annual Meeting of the American Medical Association, Philadelphia, June 11, 1931.

formations are not always restricted to the groups mentioned, yet the division is true to form in such a large proportion of cases as not to present insurmountable obstacles to the use of such a simple classification. Variations are noted, however, with sufficient frequency to turn our attention to the study of their possible explanation.

Naturally, the first approach must be through the etiology. Much has been surmised, many hypotheses suggested and a considerable amount of real investigation done without, it must be admitted, answering the question satisfactorily. Much progress has been made, however, in the proof that earlier theories must be abandoned and the establishment of basic principles that show the way to a possible solution. Too often the earlier writers have taken single examples—such as polydactylism or amputations—and have sought a simple explanation of these, overlooking the fact that the case at hand might be complicated by other lesions not permitting of the same explanation, as for example, the common occurrence of polydactylism with syndactylism, partial amputations with syndactylism. In other words, the subject has often not been considered as a whole, for when even a cursory examination is made of any considerable number of cases it is evident that few patients present lesions that are simple clinical entities. One may not presume to say that a single etiologic factor may be found for all congenital malformations; in fact, it seems probable that this is not true. It is certain, however, that some basic factor or factors affect groups of lesions.

The Ahfield theory of amniotic adhesions as the cause of amputations and polydactylism has found wide credence, although there is little to support it. Lineback reported unilateral polydactylism in a 22 mm. fetus. It is manifest that no amniotic band would be capable of splitting the digit of such a fetus. Such an assumption is incompatible also with the fact that polydactylism is generally found on both the hands and feet; that the digits involved are generally the first and fifth, and finally, that the condition is generally hereditary. Every investigator of note has concluded that amputation by amniotic bands, if it occurs, must be very exceptional. Dr. G. L. Streeter recently made an exhaustive study

Among over 8,000 specimens of the Carnegie Collection nine exhibit various stages of this phenomenon (amputation). From a study of these there is no evidence that the process is due to amniotic bands. Apparently structures described as amniotic bands fall into two catagories: (*a*) macerated sheets of epidemis; (*b*) strands of exuded fibrous tissue originating from localized necrotic areas of the superficial mesenchymal tissues.

The active stage of the phenomenon occurs about the middle of pregnancy and consists primarily of mesenchymal necrosis. It either involves the ends of one or more digits or is limited to an annular area partially or completely surrounding the extremity higher up. If enough tissue is involved, amputation ensues and the stumps heal by granulation. Where the process is more limited a sharp crease is left corresponding to the destroyed area.

The phenomenon is limited to the limb bud tissues and tends to be symmetrical in the sense of involving all four extremities, although the parts affected are usually at different levels.

of congenital amputations which will be published later. The following abstract is quoted from his work:

This is at least an advance. The explanation of the mesenchymal change may be difficult to find, and indeed the process may be open to further study, but it at least definitely removes the amniotic theory from serious consideration. In this connection the experiments of Bagg, to be mentioned later, are extremely interesting.

The atavistic theory of polydactylism and the archipterygial theory of Gegenbaur found spurious support from hasty deductions made on isolated paleologic forms of life. The well known recession of digits in the horse, deer and other mammals, coupled with the fact that in the human foot the smaller toes are apparently also undergoing recession, gave sufficient grounds for the belief that other digits might have been lost. For example, Pfitzner, in a study of 1,500 patients, found that one-third had two phalanges in the little toe, and Hasselwander found that 80 per cent of Japanese had a similar reduction. The predilection of congenital deformities for the ulnar side of the hand further supported the theory. Bardelaben contended that the progenitors of the mammalia possessed seven digits, basing his assumption on the theory that certain mammals, the whale, for instance, has more than five digits. Embryology proves, however, that the sixth digit of the whale appears some time after the typical five digits. Prentiss,[1] and others also, in extensive studies of the embryos of pigs and other mammals, controverted the theory in a convincing manner, and, finally paleontology proves that the forerunners of the mammalia were pentadactylous.

The archipterygial theory of Gegenbaur originated in the discovery in Bavaria in the deposits of the Jurassic period of two specimens of the earliest known bird (fig. 1 *A*). The bones were well preserved. It had reptilian features, teeth in its jaws, long lizard-like tail, claws on three digits—thumb, index and middle fingers—the ring and little fingers being represented by a half made wing. The second stage is represented by the still existing hoactzin (fig. 1 *B*), a bird still found in British Guiana, with an atypical thumb and index finger, the middle, ring and little fingers being a typical wing. The well known bat has an atypical thumb, with the wing made up from the four fingers. However, the studies of Beebe and others show that in the first three weeks of the hoactzin's life there is a marked regression of the digits. These observations that the claw wing is a progression from the amphibian and sequential to a fore extremity rather than a predecessor have relegated the archipterygial theory of congenital deformities to oblivion.

1. Prentiss, C. W.: Extra Digits and Digital Reductions, Pop. Sc. Monthly **68**:336, 1906.

The study of human embryos throws some light on the development of the hand as shown by the work of Bardeen and Lewis [2] on the Mall embryos. Lewis shows that by the fifth week the cartilaginous base of the bones is well laid down (fig. 9), the ulna and radius are well formed, but the fingers and wrist are as yet not well differentiated.

The theory of germ plasm origin is suggested by the fact that patients with malformation of one hand so often show involvement of other extremities in similar deformities and that frequently a hereditary history is obtained. Weighty support to this theory is given by the recent work of Bagg, Little, Müller and others, although experimental proof and clinical reports may be presented to show that injury to the buds can occur later.

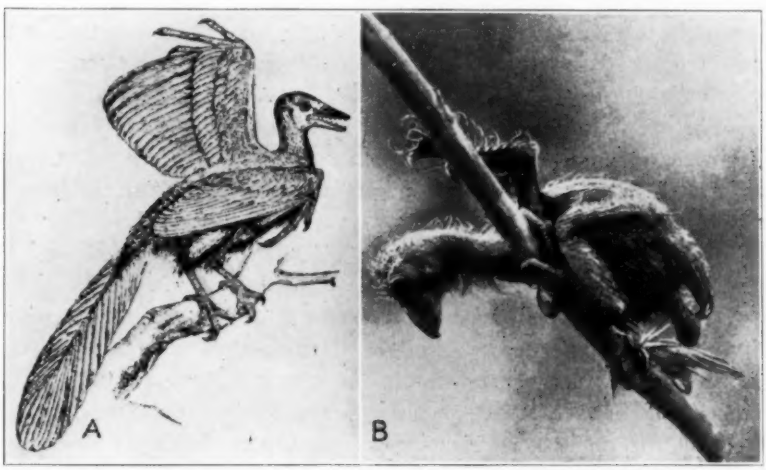

Fig. 1.—*A*, the archaeopteryx. (After William Leche, from J. Arthur Thomson: Outline of Science, New York, G. P. Putnam's Sons.) *B*, nesting hoactzin climbing with fingers and toes. (From Beebe, Hartley and Howes: Tropical Wild Life in British Guiana, New York, New York Zoological Society.)

The work of Bagg [3] stands out as one of the great contributions to our basic knowledge of this subject. It is great because it proves that congenital deformities may be produced by injury to the germinal cells, that these deformities may be transmitted through succeeding generations, and in that it permits the study of their development throughout fetal life.

2. Bardeen, C. R., and Lewis, W. H.: Development of the Limbs, Body Wall and Back of Man, Am. J. Anat. **1**:1, 1901.

3. Bagg, H. J.: Hereditary Abnormalities of the Limbs, Their Origin and Transmission: II. A Morphological Study with Special Reference to the Etiology of Club-Feet, Syndactylism, Hypodactylism, and Congenital Amputation in the Descendants of X-Rayed Mice, Am. J. Anat. **43**:167, 1929.

Mice were subjected to x-ray exposure and later bred. Among the congenital deformities appearing were those of some of the extremities. The mice showing this deformity were interbred, and the series followed for nineteen generations with suitable study of control animals. In some the fetuses were removed by operation from the uterus, examined, and in some cases marked and returned to the uterus to be recovered later at normal delivery. Over 5,000 have been studied in the inbred series; 413 had foot defects, 300, club feet with syndactylism; 9, syndactylism alone; 27, hypodactylism; 16, congenital amputations and 93, polydactylism. Out of the study of this rich material has come a knowledge of at least one manner in which these deformities may develop.

Among Bagg's conclusions are the following:

> The earliest foot defect is associated with the formation of a blister-like bleb, which raises the epithelium of the foot usually in a localized area. This condition is usually found during the twelfth to the fifteenth day of prenatal life, and is followed by the escape of blood into the bleb and the formation of a localized blood clot. These blood clots may persist until birth (fig. 2).
>
> The extent of the pathological process and its anatomical location determine whether the later-developing foot is to show either congenital amputation, clubbing, hypodactyly, polydactyly or syndactyly.
>
> Polydactyly in my experimental strain of animals may also be an expression of a localized arrest in embryonic development.
>
> Abnormalities of the limbs are definitely inherited. They are recessive to the normal in inheritance. When considered as one of the manifestations of a general tendency to abnormal structure, they approach the Mendelian expectation in behavior.

Valuable as this work is, it leaves unexplained, nevertheless, some of the phenomena of deformities, as, for example, hyperplasia. Nor has it progressed far enough to establish the connecting link between the injury of the germ plasm and the lesion in the bud. Is the process a metaplasia of cells of the part involved or is it secondary to an injury of the vascular or nervous system originating in the germ plasm? One must still speculate as to the factors that lead to injury of the germ plasm in the human embryo, although it has long been a theory that certain toxins may be causative factors. Furthermore, the isolated examples of congenital deformities that seem to have no hereditary history must be explained.

While one stands on rather firm ground as to the probability of most congenital deformities having their origin in the germ plasm, and the work of Bagg suggests the manner in which this occurs in the developing extremity, the known predilection of these deformities for certain parts of the forearm and hand is yet to be explained. The investigations of Lewis on the human embryos demonstrate the early formation of the ulnar and radial buds. The wrist and hand, however, appear but as an undifferentiated end-plate. It is possible that more intensive

study of cell groupings in the wrist and hand in embryos may be of aid, but so far such findings are not available. With two distinct buds in the forearm, ulnar and radial, one can understand how destruction or metaplasia of these primary buds will explain congenital absence, reduplication, deformity and synostosis of the ulna and radius as seen in clinical cases (see figs. 7, 8 and 29). It will also explain the associated changes seen in the hands if one remembers that certain digits are directly or indirectly outgrowths from these two buds. The phylogenetic history of the hand is shrouded in mystery, and one should regard investigations as to the development of the arm of lower forms of life as interesting but by no means conclusive. However, it is interesting to see how easily the deformities of the hand and fingers may be explained if one assumes this phylogenetic history and believes with

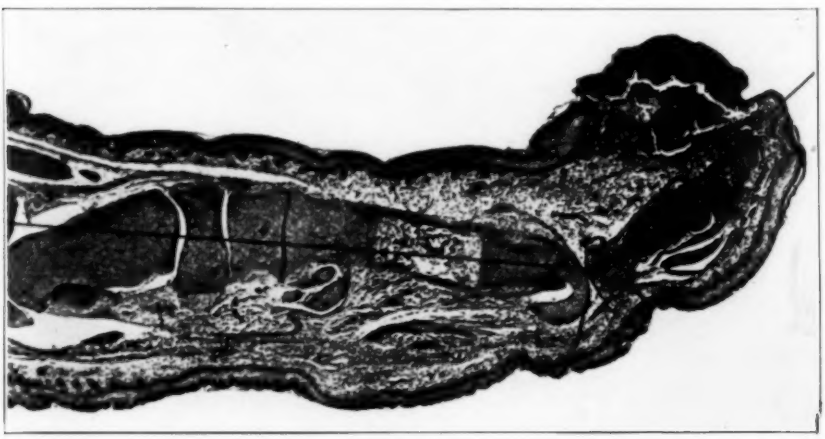

Fig. 2.—Section from the foot of a 1 day old mouse. Note the remnant of an old blood clot and destruction of the cutaneous epithelium. (From Bagg: Am. J. Anat. **43**:167, 1929.)

von Baer that "the history of the individual represents the history of the species."

The investigations of Götte and Strasser on Triton larvae, Wiedersheim on Proteus larvae and later investigations on Amphioxus and other low forms of life are suggestive at least. As Goldmann [4] stated, these investigations seem to indicate that at a certain period of its development, the carpus consists of three parallel tissue rays splitting into several parts (carpal bones) from which respectively the "radial" and the "medial" continue into the first two digits. From the "ulnar" ray, which arises secondarily from the ulnar bud, the basal elements of the third digit are derived, and rays accessory and subsidiary to this form the fourth and fifth digits.

4. Goldmann, E. E.: Beitrag zur Lehre von den Missbildungen der Extremitäten, Beitr. z. klin. Chir. **7**:239, 1890-1891, 2 pl.

Thus, in the beginning, the first and the second digits are constructed, later the third is formed and still later the fourth and the fifth. If one wishes to introduce ontogenetically the terms "chief" and "accessory rays" which are used in comparative anatomy, one has to consider the rays projecting into the two first digits as chief rays of equal value, while the other fingers together with their carpal elements should be interpreted as lateral accessory buds of the second chief ray with the qualification that the fourth and the fifth fingers are branch buds of the accessory ray passing into the third finger. The schematic drawing presented (fig. 3) illustrates an arbitrary composite picture of the results of these investigations.

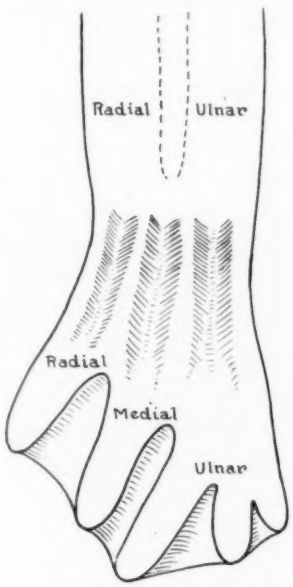

Fig. 3.—Schematic representation of the development of the hand drawn to represent combined observations of Wiedersheim, Götte and Strasser and other investigators.

The thumb originates directly from the radial bud. The middle, ring and little fingers originate from the ulnar bud, while the index lies between the two and may be involved with either in deformities although it is more closely associated with the ulnar bud. Congenital defect of the radius most often involves the thumb alone. In our two cases of congenital absence of the ulna, the thumb and index fingers were both preserved. Herschel claimed that in those cases showing an absence of the radius with a normal hand, one is dealing with a fusion of the ulna with the radius. The thumb separates first from the end-plate; and this is another reason why it is less often involved in a common lesion. The medial bud (index finger) and later that of the third finger

assume independence and must be regarded as more or less equal, while the fourth and fifth represent subordinate buds of the ulnar ray.

The earliest known footprint, that of the Thinopus antiquus found in a slab of uppermost Devonian sandstone, corroborates, according to Professor Lull, the origin of the radial and ulnar sides of the hand from different buds. We are inclined, however, to believe that Dr. Morton's deductions are more probable and that the divisibility of this paleologic foot into two parts is not fully proved. This is discussed in the section dealing with lobster-claw hand. In the living chameleons, this division of the hand into ulnar and radial elements is found.

Our own anatomic and functional studies of the hand support the theory of development as depicted in the schematic drawing (fig. 3). Anatomically, ulnar and radial divisions are found definitely separated by a fibrous partition attached to the middle metacarpal bone.[5] The tendon and tendon sheath of the middle finger are associated with the ulnar space. The index tendon and tendon sheath are associated with the radial space and entirely separated in the palm from the associated little, ring and middle finger ulnar group, but it does become associated with this group at the wrist in a common sheath. The thumb tendon and tendon sheath are completely separated from the four finger tendons and their sheaths throughout their length. This is the exact picture one would expect to find if their origin is that postulated from the embryologic studies mentioned.

A glance at the typical distribution of the vascular and nerve supply supports the assumption that the little, ring and middle fingers are closely associated; that the index finger, though separated, has a closer association with this ulnar group than the thumb.

Functionally, the same picture is seen. The thumb acts independently and the three ulnar fingers together, but in association with the index finger. The proximal flexion function crease on the palm subtends the thumb action, the distal that of the three ulnar fingers and the middle that of the four fingers.

Whether or not this is the true life history of the hand, it is interesting to see that most deformities can be brought into accord with the theory. There is a tendency to certain associated lesions, a predilection of deformities for certain parts of the hand and a predisposition for other parts to escape involvement. For example, the little and ring fingers are most commonly involved together (see figs. 8 and 29). Not infrequently the middle finger joins with them in the distorted picture. Less frequently the index becomes simultaneously affected (see fig. 19). The thumb is seldom involved with the other fingers, and when it is involved the fingers generally escape although at times the index finger joins in the changes (see figs. 7 and 10). In other words, the thumb,

5. Kanavel: Infections of the Hands, ed. 5, Philadelphia, Lea & Febiger, 1925.

index and middle fingers are more liable to individual variations; while the little and ring fingers have a tendency to common involvement frequently in association with the middle finger, less often are the four fingers involved. The not infrequent absence or duplication of the thumb alone is noted in passing; the preservation of the thumb and index fingers in absence of the ulna (see fig. 8); the frequent syndactylism of the lesser fingers, the more common appearance of brachydactylism in the little and ring fingers (see fig. 25); the preservation of the thumb and index finger and the little and ring fingers in lobster-claw hand (see figs. 13 to 18), and the infrequency of lobster-claw hand due to isolated absence of the ring finger. These and other clinical pictures fit the suggested embryologic development of the hand with sufficient accuracy to give a basis for further study, yet one must not assume that the phylogenetic history outlined is a complete explanation of all the congenital malformations of the hand.

In most congenital deformities the hereditary tendency is so well known that it hardly merits discussion. Cushing collected the histories of 302 patients with congenital ankylosis of the proximal and middle phalanges (symphalagism), 25.8 per cent in one family; DeForest Willard reported lobster-claw hand in 15 of 22 children in one family, and in 24 of 80 in another family in three generations; Marshall reported congenital amputation of fingers at the proximal phalanx that ran through four generations; Kellis studied a family of ten generations in which the thumb only was normal, while in all cases other fingers, either two or at least one, showed one phalanx absent; Mohr and Wriedt observed six generations with brachydactylism of the middle phalanx of the index finger. The hereditary nature of syndactylism and polydactylism is too well known to justify comment. The experimental production of hereditary defects in mice by Bagg and Little has already been mentioned. Its presence in other mammals is well known. Stockard and Papanicolaou studied over several years hereditary polydactylism in a strain of guinea-pigs, and they believe that it is inherited as a mendelian dominant. Prentiss concluded from his study on various animals that it is not a recessive characteristic. On the other hand, Brandeis, from a study of polydactylism, expressed the belief that the evidence is not conclusive as to its dominant character, and some things indicate it may be recessive.

While in a majority of cases the evidence seems conclusive that the activating genesis of congenital deformities lies in the germinal cell, yet one must consider the manner in which this activation manifests itself, and whether or not the process may not arise in the buds from other causes than a germinal source.

Here one still falls into the realm of pure speculation. May not a toxin affect either the germinal cell or the cells of the buds? May not the effect be produced through involvement of the vascular system or

the nervous system by direct involvement of these systems in the early stage or their elements in the germ cell or the trophic centers for these systems? The experiments of Bagg postulate a resultant destructive lesion. This does not explain hypertrophy. Hypertrophy of the thumb and index finger alone, of the middle finger to the exclusion of the remainder of the hand and other lesions may have some other explanation. The vague "inherent tendency to growth" and "physiologic growth energy" mean nothing. Valtz thinks that there may be abnormal growth of basic vessel plasm, and the observations of Orlow, von de Rothschild and Brunner seem to support this "osteitis vascularis" as do the pigmentation and hyperemia of the skin in the case of Valtz, although the pigmentation may be due to trophic nerves. Similar pigmentation in partial giant growth has been observed by Wiedermann, Manasse and Grünfeld.

Davida found, in a case of rudimentary development of the forearm and hand, an atrophy of the sixth, seventh and eighth cervical nerve centers and spinal ganglions. Edinger observed similar changes. Strauss [6] found in the entire cervical and dorsal region of a patient with complete amputation of the arm, a relative increase of gray substance, an absence of development in the motor area, a decrease in number and irregular forms of the ganglion cells, dysplasia of the gray commissure, hypertrophy of interstitial tissue and a reduplication of the central canal. There was no especial difference in cross-section from the fifth cervical to the first dorsal so that one could only reason that the whole was a germ plasm change and not restricted to the arm centers. Songuers and Marinesco found in a congenital deformity of the middle finger of the right hand a high grade atrophy of gray substance in the first right dorsal and eighth cervical gray substance near the posterior root with interstitial connective tissue proliferation and atrophy of the cells of the anterior horn. While too much importance should not be attached to these observations, yet they should be mentioned.

Confronted with conflicting theories, confused by the multitude of single clinical observations with overlapping deformities, disturbed by the various and multiple clinical terms that mean nothing etiologically, the clinician is often at a loss to understand the individual case. The investigator also is inclined to study a clinical group rather than a basic phenomenon. We have, therefore, studied the patients presenting themselves in our clinic and gone over the literature of the various case reports to see if we might not develop some simple classification that would serve as a basis for future study. The classification presented is probably far from perfect, but considered in relation to the foregoing etiologic factors it has simplified our understanding of the deformities in the patients we have observed.

6. Strauss, A.: Case of Absence of Arms in a Child, J. f. Psychol. u. Neurol. **36**:75, 1928.

CONGENITAL MALFORMATIONS OF THE HAND

A. Moderate Growth Impairment with Disorientation
   Clinical pictures
      Hyperplasia
      Polydactylism
      Syndactylism
      Hyperphalangism
      Symphalangism
      Brachydactylism
      Clinodactylism
   Radio-ulnar and other synostoses
   Mild types of disorientation of any skeletal structures
B. Severe Growth Impairment with Hypoplasia and Aplasia
   Clinical pictures
      Amputations in whole or part
      Phocomelia
      Micromelia
      Hypoplasia and aplasia of radius or ulna and their radicles
      Hypoplasia and aplasia of digits
      Lobster-claw hand
C. Combinations of A and B

ANATOMIC DISTRIBUTION OF CONGENITAL MALFORMATIONS WITH EXAMPLES OF CLINICAL PICTURES

(*a*) Injury to arm bud
   (1) Moderate injury: Radio-ulnar synostosis
   (2) Severe injury: Amputation, phocomelia, mirror hands
(*b*) Injury to radial and ulnar buds and their radicles: Disorientation or destruction of tissue in whole or part, separately or combined

Radial

1. Moderate injury producing disorientation of tissue:
   Hyperplasia of thumb
   Double thumb
   Syndactylism, thumb and index finger
   Hyperphalangism of thumb
   Symphalangism of thumb
   Brachydactylism of first metacarpal
   Synostosis of radial carpals
2. Severe injury producing:
   Aplasia and hypoplasia of radius and thumb in part or as whole

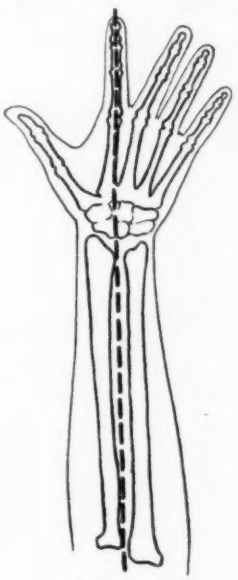

Figure 4

Ulnar

1. Moderate injury producing disorientation of tissue of fingers:
   Fingers may present:
      Hypoplasia
      Polydactylism
      Syndactylism
      Brachyphalangism
      Clinodactylism
      Symphalangism
      Hyperphalangism
      Synostosis of ulnar carpals
2. Severe injury producing:
   Aplasia and hypoplasia of ulna and fingers in part or as whole

This simple classification aids us in the orientation of our cases if it is remembered that while there is the distinct tendency for one or more of these divisions to dominate the picture, yet almost any one or more of the others may be present to some degree. Thus polydactylism, hypoplasia and syndactylism are frequently present in the same patient. The same is true of all the other clinical groups. Hypoplasia in its various forms may be the dominant picture with syndactylism, polydactylism, disorientation of tissue, etc., subordinate. Syndactylism may be the dominant picture with any of the other group subordinate. Furthermore, the radial, medial or ulnar involvement may be dominant with either of the others subordinate in whole or part. Attention is drawn particularly to this at this time so as to avoid continuous repetition of the fact when those various clinical entities are considered that appear frequently enough in a dominant form to merit individual consideration.

Table 1 presents in abstract form the data on our sixty cases.

In the 60 patients used for this study, 84 hands were involved, and these hands presented 121 so-called clinical entities: syndactylism, polydactylism, aplasia, etc. For the sake of clearness, the major clinical entities must be discussed separately, yet it is evident from these figures that they are seldom uncomplicated. The site of injury and the severity of the lesion will determine the major clinical picture. It seems wise at the present time to consider malformations of the hands and draw attention only to the fact that the simultaneous involvement of the legs and various other parts of the body is a further evidence that the source of the deformities lies in the germ plasm. In discussing our various cases, the presence of these associated lesions has for the most part been ignored since we do not wish to complicate the presentation of the subject.

HYPOPLASIA AND APLASIA

Hypoplasia and aplasia may be of any degree, from the involvement of the tip of a phalanx to that of the entire extremity. As already mentioned, in the forearm either the radial or ulnar bud or their radicles may be involved, one or the other remaining approximately normal, or both may be involved in varying degrees. The malformation may take the form of absence of a whole or part, so-called amputation, or underdevelopment with the natural form present. An isolated clinical picture may be present or the picture may be one associated with any of the other congenital malformations such as syndactylism, polydactylism or disorientation of tissue.

Certain clinical pictures are so conspicuous that when present they have received undue attention, and the fact that they are but manifestations of the same process has not been appreciated. To these have been given descriptive terms such as amputations; ectromelia,

defective arms or legs; brachymelia, short arm or leg; micromelia, abnormal smallness of part; phocomelia, absence of segments (e. g., humerus, forearm) with the hand attached to the body; hemimelia, absence of the forearm and hand, so-called ectromelia vera; ectrochiria, absence of the hand alone; ectrodactylism, absence of the fingers; brachydactylism, short fingers; brachyphalangism, short phalanges; microdactylism, small fingers; lobster-claw or cleft hand, absence of the medial part of the hand, especially loss of the middle finger and part of the metacarpal. Such terms are not objectionable unless they obscure the fact that they are all but stages of the same process. If the origin of hypoplasia and aplasia is assumed to lie in injury of the germ plasm, it is easy to understand why hypoplasia is so commonly associated with other congenital lesions and is found less commonly than other lesions as a single clinical entity. In other words, syndactylism, and even polydactylism and disorientation of tissue, are evidences of a less severe germinal injury. This is more readily understood if one bears in mind the analogy between these lesions produced by metaplasia or destruction of tissue during embryonal life and the changes seen after severe local infection and abscess formation in later life. In the latter instance, following severe inflammation without mass destruction, one sees disorientation of nerves, muscles and connective tissue with scar tissue formation on recovery. Where there has been mass destruction with abscess formation and surrounding round cell infiltration, loss of tissue at the site of the abscess with surrounding disorientation due to scar tissue is seen on recovery. In congenital lesions with moderate injury, one sees disorientation expressed in syndactylism, polydactylism, etc. With severe destructive injury, one sees hypoplasia or aplasia surrounded by evidences of less severe injury (see fig. 15), syndactylism, polydactylism, etc. In our small group, in 30 hands with hypoplasia, 18 showed syndactylism, 3 polydactylism and 4 congenital anomalies of other parts of the hand. Except in radial hypoplasia, which one would expect not to involve the fingers, there was only one hand uncomplicated by other lesions. Of 52 hands with syndactylism, 19 showed hypoplasia, 12 polydactylism and 4 other anomalies. In 20 hands with polydactylism, 12 showed syndactylism, 3 hypoplasia and 1 other lesions.

In a considerable number of the cases of hypoplasia of limbs, the history showed a hereditary tendency. Moreover, the picture of a given lesion tends to repeat itself in succeeding generations with only slight variations. Almost innumerable examples of this are recorded in the literature. Among these may be mentioned the following: Joachimsthal reported brachyphalangism and hyperphalangism of the index and middle fingers running through several generations of a family; Machal and others, brachydactylism due to a short fourth metacarpal; Mohr

TABLE 1.—*Data on Sixty Cases* *

Case	Moderate Lesion; Disorientation: Syndactylism	Moderate Lesion; Disorientation: Polydactylism	Moderate Lesion; Disorientation: Other Disorientating Lesions	Severe Lesion; Hypoplasia; Destruction; Aplasia	Lower Extremity Involved	Other Parts of Body
1	L—III-IV, dorsal flap and Thiersch graft	.....	.....	.....	L—I-II-III R—I-II, both, flap and Thiersch graft	.....
2	L—III-IV, free full thickness graft	.....	.....	.....	.....	.....
3	L—III-IV, free full thickness graft R—III-IV, free full thickness graft	.....	.....	.....	L—II-III R—II-III	.....
4	L—II-III, palmar flaps and lateral suture; should have had free full thickness graft	.....	.....	.....	.....	.....
5	L—II-III-IV, proximal flaps and suture	.....	.....	.....	.....	.....
6	L—III-IV, Thiersch graft R—III-IV, Thiersch graft	.....	.....	.....	.....	.....
7	L—III-IV-V R—III-IV-V, palmar flaps and Thiersch grafts	.....	.....	.....	.....	.....
8	L—III-IV R—III-IV	.....	.....	.....	.....	.....
9	L—II-III	.....	.....	.....	.....	.....
10	L—I-II and III-IV R—I-II-III	L—V R—V	.....	.....	.....	.....
11	R—III-IV	.....	.....	.....	.....	.....
12	R—III-IV Uncle, mother's brother, had syndactylism; cousin, son of above, had syndactylism; see case record below; bilateral	.....	.....	.....	.....	.....
13	L—III-IV R—III-IV	.....	.....	.....	.....	.....
14	L—III-IV, practically complete union of distal phalanges with one nail; tendons had common sheath; free full thickness skin graft R—IV-V	.....	L—V, lateral deviation; small and atrophic	Distal aplasia of IV-V, right	L—I-II-III-IV R—I-II, fused; III-IV-V, hypoplastic	Ears distorted; macrochilia of lower lip; appearance is that of impaired intelligence
15	L—(father) III-IV Family has history of deformity in varying degrees for some generations; two sisters, one nephew and a cousin	L—distal IV	.....	.....	.....	.....

16 Son	L—III-IV, marked distal fusion	L—III, all phalanges and part of metacarpal	.....	.....	.....	.....
	R—III-IV	R—III, all phalanges and part of metacarpal	.....	.....	.....	.....
17	L—III-IV, marked distal fusion (two cousins had extremity deformities)	L—IV, distal, middle and proximal phalanges	.....	.....	.....	Spina bifida
	R—III-IV	R—IV, distal and middle phalanges	.....	.....	.....	.....
18	L—III-IV	L—IV, partial of all phalanges	.....	.....	.....	.....
	R—III-IV Two children; one has same deformity; uncle, father and father's mother's side have same deformity	R—IV, partial of all phalanges	.....	.....	.....	.....
19	L—III-IV	L—IV, partial of all phalanges (x-ray picture not clear)	.....	.....	.....	.....
20	R—III-IV	R—IV, partial reduplication of all phalanges	.....	.....	.....	.....
21	L—II-III-IV-V	.....	.....	.....	L—I-II-III	.....
	R—II-III-IV-V Both hands, III-IV-V, close fusion of distal phalanges; others, skin only; II-III, skin only	.....	.....	.....	R—I-II-III	
22	R—II-III-IV, marked distal fusion; web proximal	.....	.....	Nail of middle finger missing	R—toes webbed; one short	Constricting band about calf of right leg
23	R—I-II-III-IV-V, complete; II-III-IV-V, most marked	.....	.....	R—I-II-III-IV-V; II, distal aplasia; III, proximal phalanx present; IV, middle phalanx rudiments present; V, distal phalanx absent; I, distal phalanx absent	.....	.....
24	L—II-III-IV-V	.....	.....	L—II-III-IV; rudiments proximal phalanges; very small rudiments middle phalanges; distal phalanges absent; V, hypoplasia of middle phalanx (clinodactyly)	.....	.....

* The Roman numerals refer to digits in order; R, right; L, left.

TABLE 1.—*Data on Sixty Cases*—Continued*

Case	Moderate Lesion; Disorientation			Severe Lesion; Destruction; Hypoplasia; Aplasia	Lower Extremity Involved	Other Parts of Body
	Syndactylism	Polydactylism	Other Disorientating Lesions			
25	L—I-II-III, complete R—I-II-III-IV, complete	.....	.....	L—I-II-III; metacarpals normal; proximal phalanx I, rudiment; proximal phalanx II, nearly normal; proximal phalanx III, normal; middle phalanx I, absent; middle phalanx II, absent; middle phalanx III, rudiment; distal phalanges I-II-III, absent R—I-II-III-IV; metacarpal normal; proximal phalanx I, rudiment; proximal phalanges of II-III-IV, fairly normal; middle and distal phalanges all absent	.....	.....
26	L—I-II-III-IV-V, complete soft tissue fusion	.....	.....	L—I-II-III-IV-V; metacarpals I and V, atypical; II-III-IV, normal; proximal phalanges I-IIand IV-V, absent; present in III; middle and distal phalanges absent (all)	.....	.....
27	L—I-II-III-IV-V; II-III-IV-V most marked	.....	.....	L—II-III, short; some phalanges probably hypoplastic; no x-ray picture	.....	.....
28	L—II-III-IV-V	.....	.....	L—III-IV, rudiments of proximal phalanges only; middle and distal phalanges absent (In this case hypoplasia is the marked picture; syndactylism insignificant, fingers distorted toward defect)	....	.....

29	L—I-II and IV-V R—I-II and IV-V	.....	.....	L—III most marked; proximal phalanx lies transverse; middle and distal absent; IV, all phalanges distorted; V, distal absent	L—II-III-IV-V, hypoplasia syndactylism	Hypospadia; stenosis of tear ducts; hair scanty on head
30	L—I-II R—I-II	.....	.....	R—III, all phalanges absent; II, distal phalanx absent L—III, all phalanges lost, metacarpal rudiment present; IV-V, normal; I, normal; II, disorientation R—III, all phalanges lost, metacarpal rudiment present; IV-V, normal; I-II, distorted, but fairly normal	.....	.....
31	R—III-IV L—I-II and IV-V, moderate only III-IV-V	.....	.....	R—II, all phalanges lost; III, all phalanges lost; IV, proximal and middle phalanges distorted L—III, possibly lost with reduplication of IV, but picture not clear; probably all digits present, however	.....	.....
32	R—I-II and III-IV	.....	R—V, possibly hyperphalangism	L—III, absent, also metacarpal; II, distal phalanx absent, middle phalanx rudiment; I, distal phalanx rudiment; V, either hyperphalangism or clinodactyly	L—normal R—syndactylism	Mongolism
33	L—either syndactylism of II-III or reduplication of II or rudiments of II and III present R—no syndactylism	.....	.....	L—I, normal; II, either reduplication or only two elements present; III-IV-V, absent, ulna absent; all carpals absent; fusion of radius and humerus; rudiment upper end of humerus present R—ulna absent; all carpals absent; metacarpals II-III-IV-V, absent; digits II-III-IV-V, absent; I, normal	.....	.....

TABLE 1.—*Data on Sixty Cases*—Continued*

Case	Moderate Lesion; Disorientation			Severe Lesion; Hypoplasia; Destruction; Aplasia	Lower Extremity Involved	Other Parts of Body
	Syndactylism	Polydactylism	Other Disorientating Lesions			
34	.....	.....	.....	L—I, rudiment only; V, absent, also metacarpals; no carpals	Webbed toes	Right femur short piece only; no fibula on right or left leg
35	.....	.....	.....	L—II-IV-V, absent; digits and metacarpals; unciform and pisiform absent; one phalanx of III lost; hypophalangism	.....	.....
36	.....	.....	.....	L—II-III-IV with metacarpals lost; I-V, distal phalanx lost	.....	Pectoralis major lost
37	.....	.....	.....	L—II-III-IV-V, digits and metacarpals absent; skin rudiments present; I metacarpal absent; unciform and pisiform absent	.....	.....
38	.....	.....	.....	L—I, distal phalanx absent; II-III-IV-V, digits absent except for rudiment of proximal phalanx of III	.....	.....
39	.....	.....	.....	R—I-II-III-IV-V, digits and metacarpals absent; skin rudiments and carpals present	.....	.....
40	.....	.....	Symphalangism L—V, proximal and middle phalanges	L—II, distal phalanx absent; III-IV, distal, middle and most of proximal phalanges absent; V, distal phalanx absent	.....	.....
41	.....	.....	.....	R—I, rudiment of digit only	.....	.....
42	.....	.....	.....	R—radius diaphysis absent; epiphyseal rudiments present	.....	.....
43	.....	.....	.....	R—radius absent; thumb absent; radial carpals and metacarpal absent; lower end of ulna atypical	.....	.....
44	.....	L—I	L—I, triphalangism	R—lower ⅔ of ulna absent; III-IV-V, digits and metacarpals absent; ulnar carpals absent L—lower ⅔ of ulna absent; III-IV-V, digits and metacarpals absent; II, normal; I, polyphalangism and polydactylism	.....	.....

45	.....	.....	.....	L—amputation at upper fourth of forearm R—II-III-IV-V, hypoplastic	.....	.....
46	.....	.....	R—I-II, metacarpal brachydactylism	.....	.....	.....
47	.....	.....	R—IV, metacarpal brachydactylism	.....	.....	.....
48	.....	R—V, rudiment L—V, rudiment	.....	.....	.....	.....
49	.....	R—V, rudiment L—V, rudiment	.....	.....	.....	.....
50	.....	L—I, rudiment	.....	.....	.....	.....
51	.....	R—I, polydactylous	.....	.....	.....	.....
52	.....	L—mirror hand present V-IV-III-II-II-III-IV-V; double ulna; partial reduplication of humerus	.....	L—radius absent; I with metacarpal and carpals absent	.....	.....
53	.....	.....	R—radio-ulnar synostosis L—radio-ulnar synostosis	.....	.....	.....
54	.....	.....	R—ulnar abduction of II-III-IV-V L—same	.....	.....	.....
55	.....	.....	R—Claw-hand appearance as if hypoplasia of muscles supplied by ulnar and median nerves	.....	.....	.....
56	.....	.....	R—III, disorientation of proximal interphalangeal joint; subluxation with connective tissue contracture	.....	.....	.....
57	.....	.....	R—V, clinodactyly L—V, clinodactyly; children have same defect	.....	.....	.....
58	R—III-IV L—III-IV	.....	R—III-IV, distal two phalanges distorted R—V, clinodactyly L—V, clinodactyly; mother and brother have clinodactyly	.....	.....	.....
59	.....	.....	L—II, macrodactyly due to neurofibromatosis	.....	.....	.....
60	.....	.....	.....	Amputation upper fourth of left forearm	.....	Amputation both legs at upper third

and Wriedt, brachyphalangism of the middle phalanx of the index finger in six generations. A particularly high percentage of hereditary histories is found in cases of split hand (lobster-claw hand); Haim found this reported in 27 of 67 cases; in 180 patients with split hand and ulnar ectrodactylism, Lewis and Embleton found all but 13 to have such a history. The list might be prolonged indefinitely, especially in hypoplastic malformations of the hands. In complete amputation above the wrist or massive involvement of the arm, such a history is less often elicited.

AMPUTATIONS

Attention has already been drawn to the fact that the commonly accepted theory that amputations are due to amniotic bands has little support and that the investigations of Bagg and Streeter tend to disprove the theory. That Wilkinson found an amputated foot in the vagina at birth, Fitch a foot, Martin a hand and Vassel a whole arm can be as easily explained as due to an intrinsic as an extrinsic cause. The fact that a history of heredity is seldom found in the case of major amputations is offset by the fact that one frequently finds associated congenital anomalies. For example, Badescu reported an entire absence of the left arm and a part of the scapula with absence of the third to the fifth toes and syndactylism of the first and second toes; Parker reported a bilateral amputation through the humerus associated with a left club foot with syndactylism, the right leg 9 inches (22.86 cm.) shorter than the left due to a defect of the femur and an absence of the fibula and four toes. Amputations of the fingers and parts of the hand have, in a large percentage of cases, some associated lesion involving the remainder of the hand. A survey of our own patients with aplasia (table 1) presents numerous similar examples. Furrows are found in every part of the extremity from the fingers to the arm, and they are not infrequently multiple and may be of any degree from a simple band of scar tissue to deep furrows of constricting scar tissue leading to atrophy or loss of the distal part. They may be present alone or in conjunction with other malformations. Goffe reported a constriction of the right forearm as if from a band, but a malformed left hand was present. Abbe reported an amputation of the distal phalanges of the thumb, index and ring fingers, and at the base of the fingers a deep groove in the skin and a similar groove encircling the palm of the left hand with a similar lesion of the index and middle fingers of the right, without, however, any constricting bands. Bagg demonstrated that these also are due to intrinsic destruction of tissue and not amniotic cords. Aplasia (amputation) of the entire arm may be found. Badescu reported absence of the glenoid tubercle of the scapula as well as the arm; Price, absence of all four extremities up to the glenoid and acetabular cavities. The so-called amputation has

been found at any point throughout the extremity. When it occurs in the humerus there is generally puckered skin only to be found at the tip; when it occurs in the forearm, bizarre positions of the ulna and radius are often seen with other lesions such as synarthrosis of elbow joints and unequal aplasia of the ulnar and radial elements (figs. 5 and 6). At the wrist the lesion loses its appearance of a typical amputation, and most frequently skin rudiments of fingers are found in spite of an entire absence of all intervening tissue.

This same picture may be found throughout the extremity. Thus Dumeril and Barton reported cases in which the arm and forearm were

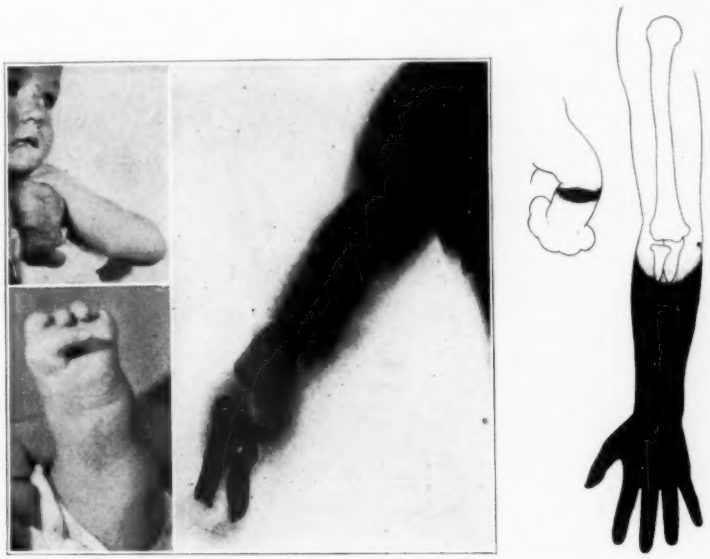

Fig. 5.—Amputation of the forearm (left) and hypoplasia of the fingers (right) with schematic drawing showing the manner of the amputation in case 45.

absent and the hand was attached to the shoulder; Flashlaid, Isenflaum and Stiell, cases in which a rudimentary hand was attached to a rudimentary humerus, the ulna and radius being absent; Chiariello and Bauchard, skin rudiments of fingers attached at the elbow; Levy, Moreau, Aburel and others, rudiments of fingers attached to the forearm or at the wrist. A similar case is illustrated in our series (fig. 6).

One may find the hand and arm well formed with absence or hypoplasia of either or both radial or ulnar elements. The hand may be involved with or without the forearm elements. The lesion is frequently bilateral. Manifestly, the picture is one of aplasia or hypoplasia, and the varied picture is but an expression of the varied intensity and location of the lesion. The hypoplasia may take the

milder form of simple disorientation of tissue. The elbow joint may present lax ligaments with a dislocation of a deformed ulna or radius, deformities of the articulatory surfaces or synostasis of one or more of the bones with varying degrees of hypoplasia of the ulna and radius and their radicles and the associated soft parts.

Two clinical pictures present themselves conspicuously, and these have been described under the titles, "Absence of the Radius" and "Absence of Ulna." There is some justification for this since the hypoplasia of a radial or ulnar bud does present a typical general picture, although it may vary in the degree of involvement of the part. It should be remembered, however, that there may be overlapping of these two pictures varying with the degree of involvement of the two buds or their radicles.

A B

Fig. 6.—Amputations at the carpus with the rudiments of fingers present in cases 37 and 39.

Absence of the Radius, Radial Hypoplasia.—Bernacchi reported that in 1,851 patients with congenital malformations, two of four congenital club hands were due to absence of the radius. Tubby alone, however, observed 11 cases and said that he sees about 3 cases yearly at the Royal Orthopedic Hospital in London. Antonelli collected 114 cases up to 1904 and Kato 253 cases up to 1923. In table 2 are analyzed the cases from Kato's [7] admirable contribution.

Four patients with absence of the radius have been observed by us. In one, referred to us by Dr. Boddiger, there was a failure of development of the diaphysis of the radius. The epiphyses were normal, and

7. Kato, K.: Congenital Absence of the Radius; With Review of Literature and Report of Three Cases, J. Bone & Joint Surg. **6**:589, 1924.

from each of them grew a rudiment about 3 inches (7.8 cm.) long that decreased in size as they approached the center of the forearm. There was some radial deviation of the hand, but no marked clubbing, and function was fairly good. There were no other deformities. A bone graft from the tibia was inserted, impinging on the grooved ends of the two rudiments. This fixed the hand in approximately normal position (fig. 7 *a* and *b*). The healing was satisfactory, and when the patient was seen some months afterward the result seemed entirely satisfactory. Unfortunately, the patient was lost sight of and no subsequent x-ray pictures could be secured. This patient represented one of the smaller groups of these cases, that of diaphyseal hypoplasia. A roentgenogram of the second patient's arm is show in figure 7.

In general, we find one of four types: (*a*) complete absence of the radius, (*b*) a rudiment of the upper end with more or less of the dia-

TABLE 2.—*Analysis of Two Hundred and Fifty-Three Cases by Kato*

	No. of Cases	Percentage
Bilateral, complete absence of the radius	107	46.1
Unilateral, complete absence of the radius	98	38.8
Right	53	21.5
Left	34	13.5
Not stated	11	4.7
Bilateral partial absence	4	0.8
Unilateral partial absence	28	11.1
Right	10	4.4
Left	16	6.3
Not stated	2	0.4
Bilateral mixed, one side complete, other partial	4	0.8
Males	104	40.9
Females	63	25.0
Not stated	86	34.1

physis present, (*c*) a rudiment of the lower end with more or less of the diaphysis present and (*d*) absence of the diaphysis.

The commonest type is, as shown in table 2, complete absence of the radius or at least the presence of only a small rudiment of the upper end of the radius. The uncommon types are those in which the diaphysis or upper end is absent.

The upper rudiment, if present, is frequently ankylosed to either the ulna, the humerus or both. The ulna is usually thickened, short and curved generally toward the radial side. A double ulna was present in two cases. Hypoplasia of its upper or lower end may be found, e. g., absence of the olecranon or styloid process. The humerus often presents anomalies at the distal end, which may be broad, rudimentary or even absent. In the carpus the radial bones are often absent or atypical in form. The trapezium and scaphoid are frequently absent, the trapezoid less often. While any or all the bones may be absent, such an extensive lesion is very uncommon. In many instances, however, various carpal bones are noted as atypical in form. The thumb

metacarpal is very frequently absent; the others are generally present. Among the digits, absence or rudimentary form of the thumb is to be expected. In our review of the cases, in which we noted all the hands involved, we found an absence of the thumb and its metacarpal in 32 instances, absence of the thumb alone in 72 and a rudimentary thumb in 14. The fingers are generally normal; a rudimentary index finger was noted twice, and it was absent in 8 cases. The fifth metacarpal was absent once. A double thumb was reported twice, and once it was noted that the thumb had three phalanges. Syndactylism was present in 5 cases, polydactylism exclusive of the thumb in 2. It is thus seen that the typical picture in the patients with extensive involvement is that of a fairly normal hand with an absence of the first metacarpal and the thumb.

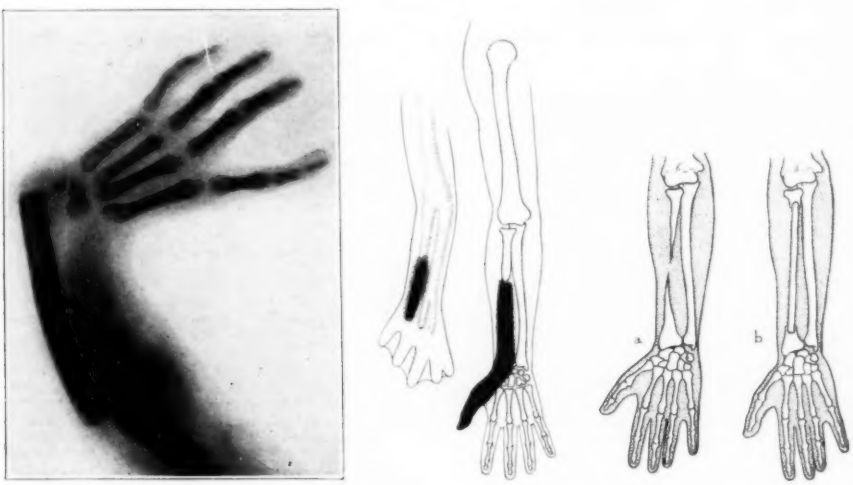

Fig. 7.—Absence of the radius in case 43. Schematic drawing showing the manner of production of radial aplasia. Aplasia of the diaphysis of the radius with a sketch of the operation performed in case 42.

The not infrequent ankylosis of the bones at the elbow joint has been noted. There may, however, due to aplasia of both the radius and the head of the ulna, be an abnormal mobility or bizarre positions.

The scapula and clavicle are at times distorted.

As regards the muscular system, it is not uncommon to find an absence of the most radial muscle bodies, or they may be disoriented, fibrosed and contracted. The biceps is often absent, while the pectoralis major and the deltoid, in common with other muscles, may be disoriented or have abnormal insertions. The radial artery is often absent, and in the forearm the radial nerve terminates in many instances at the

elbow and the musculocutaneous nerve is frequently missing. The other arteries and nerves may be disoriented.

Malformations of other parts of the body are usually present such as club foot, cleft palate, strabismus, spina bifida, anomalies of the ear and of the genital organs. Such variation naturally presents many clinical pictures: a typical picture, however, is one in which one sees general atrophy of the arm, the shoulder often small, the upper part of the arm usually fairly normal, the forearm short and distorted and curved with the convexity on the posterior side. The hand shows radial deviation, often at a right angle to the forearm, called by Bouvier "radiopalmar variety of club hand." In severe cases the medial surface of the forearm may be in contact with the hand. The hand is often small, with the thumb absent or with a rudiment loosely attached. In spite of the atrophy and distortion, the function is often surprisingly good. The articulations are generally normal, but movement is restricted because of the luxations and muscular contractures.

A hereditary tendency has been noted in some case histories, but is apparently not common. Blencke reported the condition in four children in one family, and Joachimsthal, similar deformities in a mother and five children.

Treatment: The function of the arm and hand may be improved in many of these patients by bone transplantation designed to correct the deformity and secure stability. The principles on which such operations must be carried out are: (*a*) Severance of fibrous tissue or contracted muscles holding the hand in an atypical position. (*b*) Insertion of bone either from the ulna or other bones so wedged to the ulna and the carpal bones as to hold the hand in a functioning position. Such transplants must be inserted so that the ends come in contact with denuded bone so as to favor bone growth since the simple insertion of a graft among the muscle bodies on the radial side will end in the absorption of bone. (*c*) Fixation of the hand in a functioning position with subsequent physical therapy continued for a number of months to restore mobility to distorted joints and function to atrophic muscles. (*d*) Fixation of the hand in dorsiflexion in certain cases with abnormal motion due to aplasia of the joints so as to place the hand in the position of function. In those cases in which such fixation may ensue, although not sought for, the dressing of the hand should be so applied as to maintain this position if such a result should unexpectedly ensue.

Historically, it may be mentioned that tenotomy of contracted muscles, arthrodesis of the ulnocarpal joint, simple osteotomy of the ulna followed by overcorrection (Hoffa), cuneiform osteotomy of the lower end of the ulna accompanied by section of contracted muscles (Romano), osteotomy of the ulna followed by stretching by adhesive plaster tension followed by resection of the os magnum and the uncinate and the inser-

tion of the lower end of the ulna into the cavity, the styloid having been removed (Sayre and Roswell Park), and attachment of the cut end of the ulna to the curetted semilunar with tenotomy (McCurdy) have all been carried out with only moderate success.

Bardenheuer and Antonelli have split the ulna and used the radial fragments as a substitute for the radius. In certain cases with large ulnae, this procedure may have some advantages.

Bardenheuer, followed by Tubby, split the distal end of the ulna into radial and ulnar portions and pushed a carpal bone up between the lower ends. The ends of the ulna and the new radius were fastened to adjoining carpals by an ivory peg. If the upper end of the severed fragment is permitted to remain attached to the ulna, this operation should be followed by fair success. If, however, it is completely detached, absorption is likely to ensue.

With the idea of creating a new radius separated from the ulna by muscular bodies, Antonelli split the ulna from the distal to near the cubital end, being careful to preserve intact the lower end so as not to produce ankylosis. The middle third of the ulna was then broken obliquely, and the end of the newly formed radius was attached to the ulna and carpus by wire. In a later case, he supplemented this with a plastic operation by means of a Z-shaped incision on the contracted tendons. This procedure also must be limited to a few cases in which an exceptionally large ulna is present.

The second type of bone transplant, that in which the graft is taken from a distance, is illustrated by the patients operated on by Albee, Ryerson and ourselves.

Attention has already been drawn to the fact that in our patient we supplied the diaphysis of the radius by a tibial graft (see fig. 7). The upper and lower ends of the radius were present, so that after cutting off the tapering bone and chiseling out a cavity at either end, the graft was inserted between the two ends and fixed in position by catgut sutures. No muscles were missing, so that after cutting the contracting fibrous bands we had no difficulty in inserting the graft between the muscle bodies although we could not identify accurately the individual muscles. We did, however, divide them grossly into volar and dorsal masses. The bony union of the graft with the remnants of the radius was favored by a collar of periosteum taken from the tibia and wrapped about the junctions of the shaft with the rudiments. As has been stated, at the time last seen some six months after the operation, the result was entirely satisfactory. The position of the hand was improved, unnatural mobility had been corrected and the function was excellent. Unfortunately, the patient was then lost sight of so that the ultimate result cannot be stated.

Albee, in a patient with entire absence of the radius, inserted a tibial graft in its place. This graft was mortised into the ulna at about its

middle and the lower end into properly prepared orifices in the carpus. A similar procedure was carried out on the other side, followed later by an osteotomy of the ulnae to correct ulnar deformity. The tissues were stretched, and an attempt was made to produce overcorrection. This patient had a high degree of radial club hand and great disability. Some years afterward, Dr. Albee had an opportunity to examine the patient.[8] The result was excellent. The patient could play tennis, drive a car, paint, etc., and roentgen examination showed a firm fixation and growth of the graft.

In a second case in which the carpus was missing the graft was mortised into the first metacarpal, and the proximal end was placed among the muscles at the elbow. The same intermuscular position of the upper end was used in a third case. It is to be feared that the two last operative procedures will not secure the excellent result of the first since they violate the principle that both ends of the graft should lie in contact with bone where possible, otherwise more or less absorption of the graft is likely to ensue. Ryerson, in his case, placed his whole graft intermuscularly, leaving the periosteum and distal epiphyseal cartilage attached to the graft. Here subsequent x-ray pictures showed the absorption of the bone that experience has taught us to expect with such transplants.

Absence of the Ulna, Ulnar Hypoplasia.—Absence of the ulna in whole or parts is found less often than absence of the radius. As already stated, Kato collected 253 instances of absence of the radius up to 1923. While we have made no attempt to make a complete collection of case reports of absence of the ulna, yet in a fairly adequate review of the literature we have found only slightly over 50 cases. In 45 of these, including our 2 cases, the case reports are sufficiently descriptive that some conclusions may be drawn as to the general picture found in this lesion.

It is interesting to note that this picture is almost an exact complement of that already described under radial hypoplasia (absence of the radius). Its complementary similarity is expressed in the short forearm, curved radius, atrophy with ulnar deflection of the hand and loss in varying degree of ulnar elements. It may be said, however, that it differs in the fact that dislocation at the elbow is more common and the destruction of digits, metacarpal and carpal elements, is greater. The ulnar deflection is not so conspicuous as is the radial deflection in absence of the radius, but the loss of function is greater due to the fact that there is so often greater destruction of hand elements. This is well illustrated in the photographs of our two patients. It was seen

8. Albee, F. H.: Formation of Radius Congenitally Absent; Condition Seven Years After Implantation of Bone Graft, Ann. Surg. **87:**105, 1928.

in the Miller-Kraft case (fig. 8) that the lesion was bilateral, the lower two thirds of each ulna was lost, the radius was curved in the radial and dorsal direction, was thick and distorted and the upper end had been dislocated to the volar surface of a distorted lower end of the humerus. Only two digits, probably the thumb and index finger, were present on the right side, and there was a probable absence of all metacarpals with only three carpals present which we would hesitate to identify. On the left side were two well formed digits, probably the thumb and index finger with a reduplication of the index finger. There was fair function present in these digits. In the Rossi case the disability

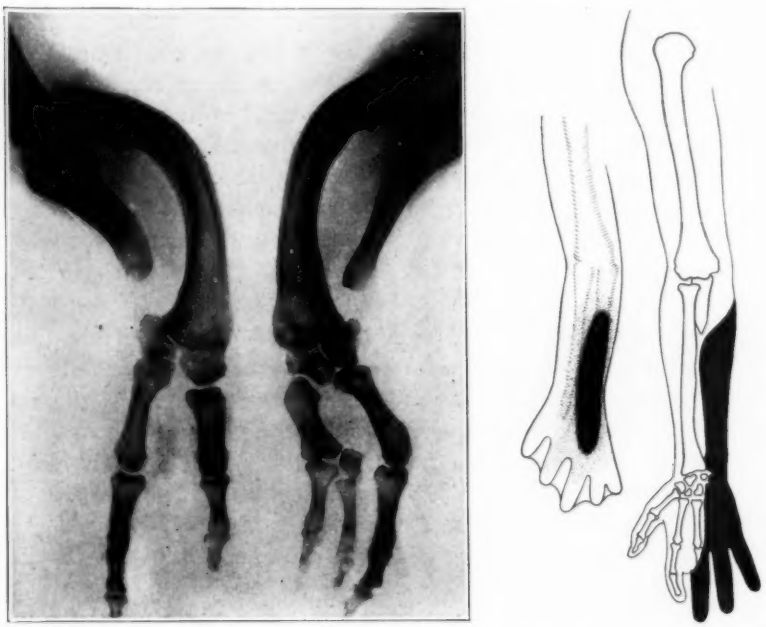

Fig. 8.—Absence of the ulna, ulnar carpals and three ulnar digits and polydactylism of one thumb in case 44 (courtesy of Drs. Miller and Kraft). Schematic drawing showing the manner of production—necrosis of the embryonal ulnar element surrounded by disorientation.

was greater. On the right side the radius was dislocated anteriorly and laterally, not so markedly deformed as in the previous case. There were a small ulnar rudiment, two metacarpals and the rudiment of two carpals. Of the two digits, one was evidently the thumb, the other possibly an index finger with rudiments of reduplicated index phalanges bound to it in syndactylism. On the left side the upper end of the radius was ankylosed to the humerus, and an unidentified single digit with its metacarpal was dislocated to the dorsal surface of the lower end

of the radius. In this case, on the right side the x-ray picture of the forearm bone was inconclusive, but by palpation the bone lay evidently on the radial side, and the presence of radially lying digits, one evidently a thumb, made us conclude that the bone lost was the ulna. Moreover, the loss of so many digits with the carpals and metacarpals is seen more often in absence of the ulna than in absence of the radius. In these hands the disability is great.

While the data on the 45 cases we have had at our disposal are often incomplete, a study of them does give a fairly accurate idea of the common findings. In 15 of these 45 patients, the lesion was bilateral. In the 60 hands there was practically total loss of the ulna in 23, the upper part was lost in only 1 and the lower part in 18; the diaphysis was absent with both ends present in 3 and both ends were lost and the diaphysis present in 1. It is noted in 9 that there was ankylosis of the radius to the humerus, and in 15 there was a dislocation of the radius upward. Its position in relation to the humerus varied. When the destruction of the ulna was not great, the hand was intact and the function excellent. In 33 hands, however, and possibly more, a loss was noted, varying with the intensity of the destructive lesion.

Absence of the carpal bones was a conspicuous part of the picture. In six it was noted as practically complete. In almost all instances of partial loss it was the ulnar bones that suffered, either the cuneiform and pisiform or the cuneiform, pisiform, uncinate and os magnum. The trapezium is noted as lost in 1 case. However, a glance at the x-ray pictures of the cases here presented will demonstrate how difficult it is to say more than that ulnar or radial bones are lost, and sometimes it is difficult to be sure of this, but that the loss of the ulnar carpals is the common accompaniment cannot be questioned. Digital and metacarpal loss are found to be what one would expect when the embryologic data and the ontogeny of the hand as discussed under etiology is remembered. One would expect to find a conspicuous involvement of the third, fourth and fifth digits and at times the second, while the first (the thumb) would be expected to escape. In the 33 hypoplastic hands, the loss is as follows: the second, third, fourth and fifth digits, 6 cases; the third, fourth and fifth, 11 cases; the fourth and fifth, 11 cases; the second and fifth, 2 cases; the fourth, 1 case, and the fifth, 1 case. The character of the digital loss is more graphically shown in classifying the loss of individual digits: loss of the fifth digit, 32 cases; the fourth, 29 cases; the third, 18 cases; the second, 8 cases; the first, 4 cases; but in 9 it was noted that the thumb showed some pathologic change, e. g., syndactylism, loss of phalanx, symphalangism. This marked predilection for extensive destruction of the ulnar digits stands out in sharp contrast with radial hypoplasia in which over a hundred hands showed involvement of the

thumb with the remaining digits normal in almost all cases, except that the index showed distortion in several cases. The discrepancy in the statistics arises from inadequate histories.

As to associated lesions, the lower end of the humerus is frequently atypical and may be short. Club foot, deformity of the scapula and absence of the fibula, patella and tibia are noted at times. Absence of the ulnar artery and nerve is not infrequent, as is also loss of the flexor carpi ulnaris and some of the muscles of the hypothenar area. Muscular atrophy is common. Syndactylism appears frequently and polydactylism at times; bifid pollex was noted twice.

We therefore portray the clinical picture as follows: The lesion is frequently bilateral, the arm often short, the elbow greatly distorted with the radius dislocated upward, the forearm short, not much flexed on the arm, atrophic, with a slight curvature to the radial and often the dorsal side. The hand, if present, is commonly in moderate ulnar deflection lying between supination and pronation (ulnar club hand, Stoffel, Stempel), but generally with good function. When the hand is involved there is often great loss including the carpals, metacarpals and digits, the maximum loss being on the ulnar side, often only one or two radial digits being present, and these with little function and not infrequently showing syndactylism. Congenital malformations may be present in other parts of the body. A hereditary history is not often found.

Treatment: When the hand is intact, the function is often so excellent as not to demand surgical intervention. With considerable loss of the ulna, however, arthroplastic procedures may be demanded at the elbow to secure mobility, although we are not aware that this has been done. Cases may also be found in which a transplant of bone may be necessary to secure stability and function. This, however, will occur in only the exceptional case, since if there is a functioning hand the deviation and distortion is not so great as in radial loss; moreover, in the case with extensive loss the hand is so often badly crippled that the restoration of the ulna will not secure a satisfactorily functioning hand. If such a procedure is carried out, it should follow on the same lines as described for restoration of the radius. At times the treatment of the syndactylism or the removal of rudimentary elements in the hand may be advisable to increase function. We, however, have had no case in which we believed surgical intervention would improve the function.

HYPOPLASIA OF HAND

Attention has already been drawn to the rather typical pictures of ulnar and radial hypoplasia in various parts of the hand which arise sequentially to a lesion in the forearm.

When one considers hypoplasia in the hand arising from a lesion primarily affecting the hand, one would not expect to find a few typical lesions, but rather a multiple of pictures arising as a result of the varying locations, degrees of involvement and periods of embryonic life at which the insult occurred. If the lesion involves the proximal part of the hand or wrist, the whole hand may be lost; if the lesion is lateral, it may be the thumb alone or any radial group or the ulnar group in part or whole that is involved. If the lesion is extensive and below the origin of the thumb, the fingers may all be involved, the thumb escaping injury; if a smaller median lesion is present the medial digits only will be affected, the lateral being normal, or finally there may be involvement of single digits in whole or part. Not only this, but the individual bones may be involved, the hand as a whole being normal. These bones may be absent or fail of proper growth (brachydactylism, brachyphalangism, absence or hypoplasia of carpal bones, etc.). Certain of these lesions have been singled out for special consideration because of the conspicuous nature of the lesion or of its frequent isolated appearance, e. g., absence of the thumb, defect of the median group of phalanges (split hand or lobster-claw hand), brachydactylism and brachyphalangism. Again it should be emphasized, however, that they are but phases of the same general process. The ontogeny of the hand, however, predisposes to certain groupings of the lesions. Due to the development of the thumb from an isolated bud it is not uncommon to have a hypoplastic thumb with the remainder of the hand normal and hypoplastic fingers with a normal thumb. Since the little finger is an accessory bud twice removed from a primary bud and is terminal, the blood supply is easily interfered with so it also is subject to exceptionally frequent involvement. The close association of the middle, ring and little fingers in embryonal life determines the frequent association of these in a hypoplastic process.

The various types of hypoplasia of the hand have certain things in common. The picture is very seldom that of hypoplasia alone. The involvement of more than one extremity is very frequent and sometimes all are involved in more or less similar lesions. A hereditary history is very common.

The associated lesions are many and varied in type and degree. One would expect this when it is remembered that a lesion leading to destruction would have around it an area of disorientation of cell growth. A similar picture is seen in an abscess where there is a local destruction of tissue surrounded by an area of cellular infiltration with ultimate scar tissue formation and structural deformity. The same process occurring in embryonal life before structural formation would certainly lead to disorientation of the developing tissue about the area of destruction

(see fig. 14). Syndactylism and polydactylism are especially common. Symphalangism, polyphalangism, brachydactylism, brachyphalangism and disorientation of tissue all appear. Any or all of these may be present in an individual case.

This association of various lesions is illustrated in our cases. In 30 hands showing more or less hypoplasia there were 18 with syndactylisms, 3 with polydactylisms and 4 with disorientation of tissue, or 55 various lesions in the 30 hands.

The hereditary nature of the lesions involving the hand alone is so conspicuous that it merits no further discussion than that already given.

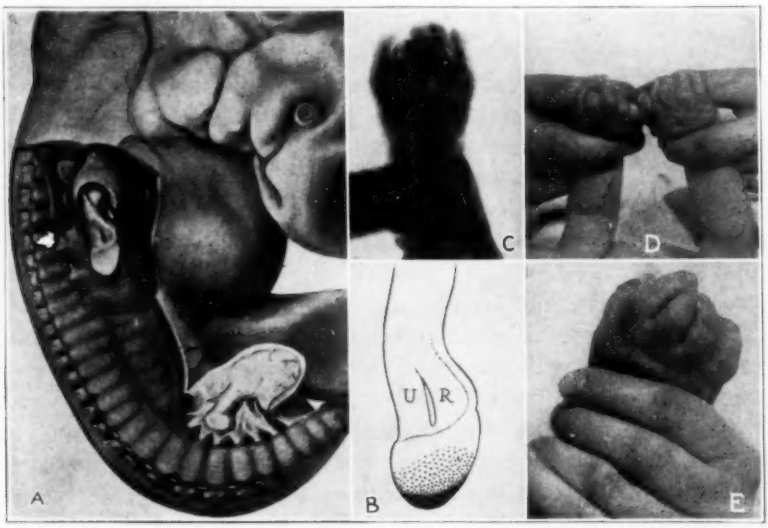

Fig. 9.—*A*, embryo (Mall) of 4 weeks, showing ulnar and radial development with undifferentiated end-plate (hand and fingers). (From Bardeen and Lewis, Am. J. Anat. **1**:1, 1901.) *B*, enlarged drawing of the ulna and radius with end-plate showing schematic distal disorientation. *C*, *D* and *E*, photographs of the hands showing result of such disorientation in cases 21, 22 and 23.

These general remarks are probably best illustrated by a short résumé of the findings in some of the patients who have come to us presenting hypoplasia of the hand as a major clinical sign.

Hypoplasia of All Elements.—Case 39.—Miss Z., referred by Dr. Pavlik (see fig. 6 *B*), had unilateral aplasia of the hand, but showed no other congenital malformations. An examination of the x-ray picture discloses an entire absence of the metacarpals and phalanges except for a rudiment of the thumb. The carpal bones seem to be intact, and from the x-ray picture one might assume it to be an amputation by an extrinsic lesion. The photograph of the hand, however, discloses skin rudiments of the digits, the first and fifth being especially noticeable.

CASE 23.—M., described as one of the patients with syndactylism (fig. 9, *C, D, E*), illustrates the type in which the terminal phalanges of all five digits are hypoplastic, the remainder of the hand being well developed except for the syndactylism.

Lateral Hypoplasia.—Complete ulnar hypoplasia is well illustrated by case 37, that of Miss E. in which there was entire absence of all metacarpals and phalanges of the fingers (see fig. 6 *A*). There was, in addition, a loss of the distal and part of the proximal phalanx of the thumb with some disorientation—fusion of the trapezium and trapezoid—present in the carpus. Again, however, the photograph of the hand shows skin rudiments of the fingers. There was function, though restricted, in the thumb.

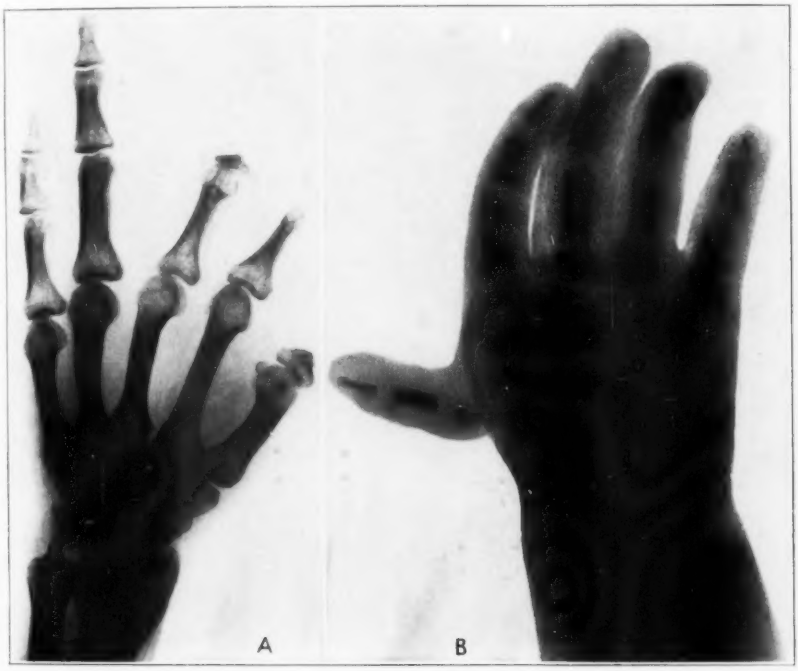

Fig. 10.—Radial hypoplasia in cases 25 and 41.

Another patient (see fig. 29 *C*) showed hypoplasia of the four ulnar digits, a loss of the distal phalanx and part of the middle phalanx of the index finger, loss of the two distal phalanges and part of the proximal phalanx of the middle and ring fingers, loss of the distal phalanx and symphalangism of the middle and proximal phalanges of the little finger. The thumb was normal with complete function; the hand otherwise normal. This picture begins to merge into that of hypoplasia of the middle part of the hand (cleft hand) to be discussed later.

It will be seen that this group of cases shows more or less involvement of most of the digits (second, third, fourth and fifth). Any single one of them, however, may be absent, although this is exceptional except in lobster-claw hand.

Radial Hypoplasia.—The typical expression is found in involvement of the thumb, as demonstrated in case 41 (fig. 10*B*). This hand was normal except for a functionless rudimentary thumb. The phalanges were small but of fairly normal outline; the metacarpal was represented by a rudiment only. The appendage was flail-like and apparently lacked muscular connection. The patient had no control over it. This then is a typical hypoplasia of a pure radial element.

More or less involvement of the radial fingers may be present, as illustrated in case 25 (fig. 10*A*). This patient had a bilateral lesion, hypoplasia with syndactylism. The right hand showed a loss of the distal phalanx of the thumb with a rudiment of the proximal phalanx. The index finger presented a fairly normal proximal phalanx with the distal phalanges absent, the middle finger a normal

Fig. 11.—Ulnar and radial hypoplasia in case 26.

proximal phalanx, rudiment of the second and absence of the third, all held together in syndactylism. The ring and little fingers were normal. The left hand presented a similar thumb and index finger. The middle finger was similar except that there was a symphalangism of the proximal phalanx with the second phalangeal rudiment. The ring finger was similar to the middle finger. The four digits were bound together in syndactylism. The little finger was normal. This patient was operated on, and the fingers separated.

Bilateral Hypoplasia, Medial Parts Less Involved.—Case 26.—The child in this case presented hypoplasia of both ulnar and radial elements, the middle finger being the least involved (fig. 11). The first and fifth metacarpals were short and had no phalanges attached. The second, third and fourth metacarpals were normal, the second and fourth had no phalanges attached, but the third had a fairly well developed proximal phalanx with a rudiment of the second. All were bound

together in syndactylism; otherwise the hand was normal. A congenital scar is seen in the photograph on the ulnar side of the forearm.

CASE 34.—The patient in this case (fig. 12 *B*) presented only digits on the left hand. They were difficult to identify. It is probable that the thumb was represented by the radial rudiment, one digit was probably the index finger, the other probably the third. This is suggested because there was a cleft between the two digits extending down into the palm, a picture similar to that seen in cleft hand with an absence of the middle metacarpal and finger. No carpal bones were seen, although they may not have as yet ossified. The wide separation of the ulna and radius from the metacarpal suggested that some might be present. Some centers of ossification were seen in the normal right carpus. Neither the metacarpals nor phalanges of the two digits present were normal, but the digits showed fair function. All other metacarpals and phalanges were lost. This patient showed also a right club foot, short hypoplastic femur, no little toe, no fibula, only four tarsal bones, two metatarsal and four toes. The right hand was normal.

Fig. 12.—*A*, ulnar aplasia in case 14. *B*, ulnar and radial aplasia in case 34. Sketches of the preoperative and postoperative condition and a photograph and roentgenogram of the hand after operation are shown for case 34. (See schematic drawing, figs. 8 and 29.)

The thumb rudiment was removed, and the cleft sutured out to the end of the metacarpals after the manner to be described in the discussion on the treatment of cleft hands. The function following this procedure was satisfactory.

Hypoplasia of Medial Elements (Lobster-Claw or Crab-Claw Hand, Perodactylus, Peromanus, Peropus, Perochirus).—By the term "medial elements," reference is made to the medial part of the hand in contradistinction to the lateral. The simpler and classic type, that of aplasia of the middle finger with part of its metacarpal has received undue attention owing to its striking pathologic picture, and some would reserve the term lobster-claw hand to this particular lesion. Even a cursory examination, however, discloses that it is but one phase of medial hypoplasia. Some authors have attempted to give descriptive names to the varying degrees of medial hypoplasia, but this is unjustified since

the variations are of degree and not kind. Every degree may be found from simple loss of the middle finger to complete loss of all medial elements with rudimentary elements of the first and fifth digits only remaining. Others have attempted subclassifications based on the position of the rudimentary metacarpals or phalanges present. This also is unnecessarily confusing since the varying position of these bones with the associated syndactylism is simply an expression of varying degrees of the associated disorientation. We will go much farther in our understanding of these cases if we disregard the unnecessary and unwise nomenclature and begin our study with the full understanding that the various types are but the expression of a greater or less degree of hypoplasia with associated disorientation.

Etiology: While we are convinced that the process is the result of local destruction of tissue having, in common with the hypoplasias already discussed, its origin in the germ plasm, yet because of its striking similarity to a picture that would appear if due to a nonunion of embryologic elements or to a reversion to the types of certain mammalian feet, these possibilities should be considered. This is particularly true if we were to confine our attention to the classic simple type of loss of the middle finger as some authors have done. The argument for reversion to ancestral type is based on the frequency with which a hereditary history is obtained, on the footprint of the Thinopus antiquus and the split foot of the lizards and salamanders.

Haim said that in 27 of 67 cases the history showed a hereditary tendency. Meyer reported a family of 20 in four generations, with 13 persons affected showing 13 split hands and 26 split feet. Lewis and Embleton found 180 individual cases, including some radial types of ectrodactylism, with a hereditary history in all but 13. In a family with 51 persons in four generations, 35 were affected. They believe, however, that it is not governed by mendelian laws and that swamping of transmitted sports will eventually take place. In reply to this, one has only to draw attention to similar histories of hereditary tendency obtained in almost all cases of hypoplasia of various degrees and of other types of congenital deformities in which no ancestral type could by any stretch of imagination be found.

As to ancestral forms, the imprint of a foot of some ancient mammal was discovered in a slab of sandstone in the uppermost Devonian stratum (Chemung) in 1896 by Professor Beecher of Yale (fig. 13 *A*). This is the earliest record of a mammalian foot. It is interpreted by Professor Lull as "presenting two completely formed fingers, probably the first and second, the cleft between them extending deep into the sole of the foot. The phalangeal pads and a rounded, terminal, claw-like portion are well developed and there appears on the outer side of the digit II the rudiment of a third—and below this the possible anlage of digit IV." While I have not had an opportunity to study this footprint,

yet I am inclined to agree with Morton, who after an examination, believes that the assumption of its form is not proved and that the footprint may be incomplete, the imprint of the other toe having been broken off and that instead of being a four toed mammal it was really true to type and had five toes and was really not a split foot.

The assumption that the split hand is a reversion to type as expressed by the salamanders and lizards cannot be dismissed so lightly. Robe studied the developing Triton, Wiedersheim presented studies in the

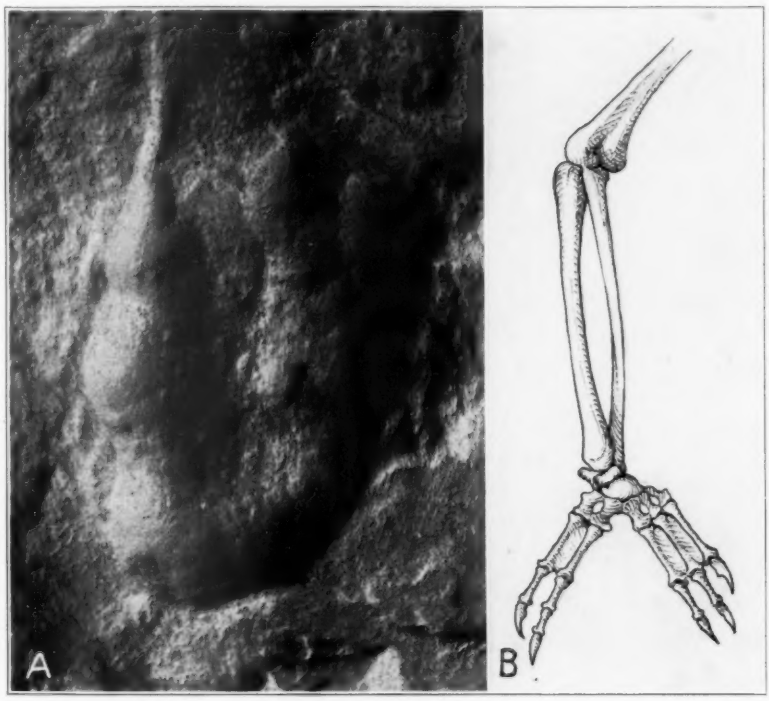

Fig. 13.—*A*, photograph of a cast of the footprint of the Thinopus antiquus (Marsh) (courtesy of Professor Lull). *B*, sketch of the bones as they lie in the foot of the Chamaello jacksoni Boulenger (courtesy of Field Museum).

comparative anatomy as shown in the Ranodon sibericus, and there are extant the chameleons giving proof of mammalian split feet. The drawing presented made from a specimen (Chamaello jacksoni Boulenger) in the Field Museum shows a foot split between the second and third digits extending almost to the carporadial joint (fig. 13 *B*).

The embryologic origin of the hand has already been discussed, and did we not have weighty evidence to the contrary, we might be inclined to believe the split foot to be a reversion to this type. This evidence lies largely in the findings that the classic middle finger loss with the hand

cleft to the wrist is but the expression of a single phase of hypoplasia and every graduation of this from a loss of less tissue, e. g., part of the third digit, to complete loss of nearly all medial elements may be seen. To our mind the similarity of the classic type to the embryologic picture and the intriguing problem of its origin has induced an undue attention to this particular degree of hypoplasia with the collection of cases presenting this phase to the neglect of other and less interesting types. Moreover, the theory does not explain the disorientation of the surrounding tissue with its syndactylism and distortion of bony structure which is such a conspicuous part of the picture (fig 14).

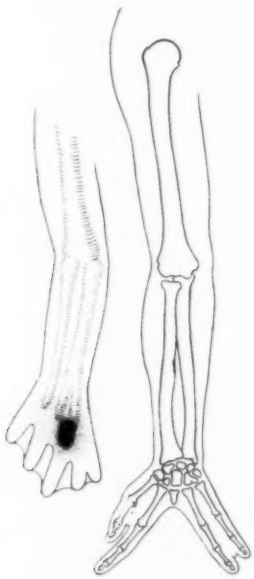

Fig. 14.—Schematic drawing illustrating genesis of lobster-claw hand following central necrosis and surrounding disorientation in the embryonal limb.

The clinical and pathologic picture in its varying degrees is well shown in the cases selected from our series.

CASE 29.—*Bilateral medial hypoplasia; left syndactylism of first and second digits; polydactylism with double proximal phalanx of first digit; feet show bilateral medial hypoplasia, right, loss of phalanges of second digit; left partial phalangeal loss of second digit; syndactylism; bilateral stenosis of tear ducts; hypospadias; premature closure of fontanels; deficient growth of hair.*

Baby H., aged 6 months, presented in the right hand the classic picture of lobster-claw with an absence of the phalanges of the third digit, the metacarpal, however, being present. The second and fourth digits were widely separated and pointed laterally rather than distalward. The thumb looked fairly normal and had good function. The index finger had two phalanges, no nail, was pointed, dis-

oriented with lateral curvature and flexion and had slight syndactylism with the thumb. The function was greatly impaired. A wide web extended over to the fourth and fifth digits. The fourth digit pointing ulnarward had a large base, partly bone and partly neuromatous tissue. Its function was good; all phalanges were present with the nail. The fifth digit was approximately normal (see fig. 15). The left hand was much more disoriented. It also presented the classic lobster-claw hand. Pathologically, the bones of the thumb were normal except that there was apparently a doubling of the first phalanx. The index finger was markedly distorted, bound in syndactylism with the thumb; the first phalanx articulated distalward with the supernumerary first phalanx of the thumb, and a distorted second

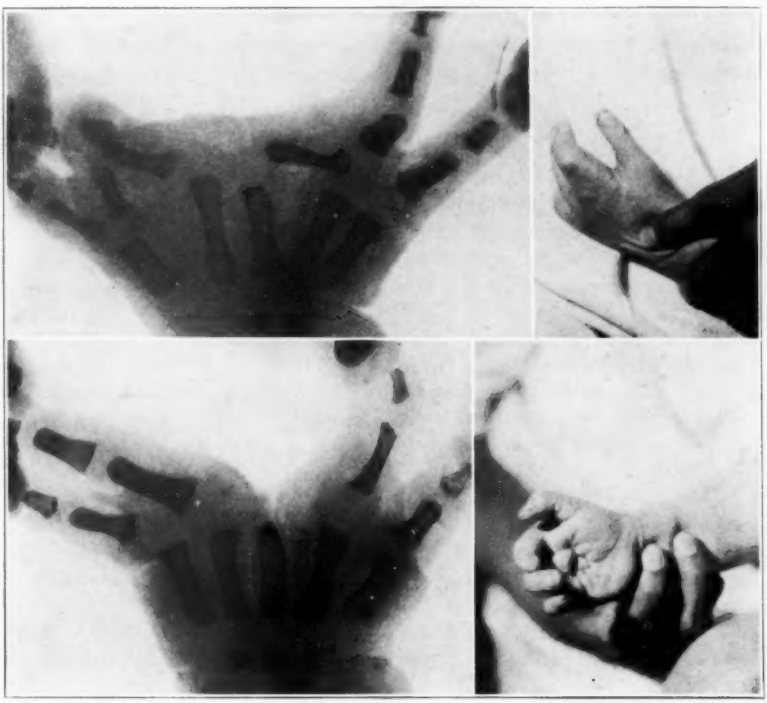

Fig. 15.—Median hypoplasia with loss of the middle finger and part of its metacarpal, bilateral, in a case of lobster-claw hand (case 29). The x-ray pictures were made before operation; the photographs, after operation.

phalanx was held in about 60 degrees radial abduction. The metacarpal of the third digit was present, and the first phalanx lay transversely, articulating distally with the metacarpal of the fourth digit and its disoriented first phalanx. The other phalanges were absent. The fourth digit was fairly normal except for the poorly developed first phalanx. The fifth digit was approximately normal.

Operation.—Due to the extensive disorientation, the operative procedure was divided into stages. First stage, right hand: An incision was made from the middle of the proximal phalanx of the ring finger on its radial side passing along the extended web to the middle of the proximal phalanx of the index finger on its

ulnar side. From here the incision encircled the proximal phalanx of the index finger near its base, the skin only being incised. The skin was now dissected from the dorsal and flexor surfaces for a sufficient distance proximalward to permit shifting of the entire index finger and its metacarpal ulnaward after adventitious bands were severed. The fascia and connective tissue was separated on the palmar surface from the metacarpal bone of the absent middle finger and three fourths of the metacarpal bone removed. A heavy catgut suture passing through the periarticular fascia then brought the distal ends of the metacarpal bones of the index and ring fingers together. A second heavy catgut suture passed in a similar manner brought the proximal ends of the proximal phalanges in close apposition. Some excess connective tissue was removed, and the edge of the skin incision sutured, dorsal surface to flexor surface. It will be noted, however, that the index finger now occupies a position more ulnarward than previously, and here, of course, the flexor skin of the palm was sutured to the flexor skin of the finger, dorsal surface to dorsal surface. This shifting of the finger, but not the skin, also provided a more extensive web between the index finger and the thumb (see fig. 24). The suturing was reinforced during the dressing by adhesive tape around the palm and around the index and ring fingers. By this means a normal palm was restored, and the fingers were held in apposition all pointing distalward as in the normal hand. First stage, left hand: An incision was made along the web transversely from the ulnar side of the index finger to the radial side of the ring finger. The palmar fascia and connective tissue were dissected free from the transversely lying first phalanx of the middle finger and its metacarpal. The phalanx and the distal three fourths of the metacarpal bone were removed. The flexor tendons going to the index finger and thumb could be seen and traction caused flexion of the thumb, but not of the index finger. A second incision was then made on the dorsum of the hand to the radial side of the first phalanx of the index finger extending one-half inch (1.27 cm.) on the dorsum of the hand and a less distance on the flexor surface. The supernumerary proximal phalanx of the thumb was removed. The connective tissue holding the distorted index finger was excised, the index finger brought over to the ring finger and the two sutured together in a manner similar to that described for the right hand. The transverse web skin incision was sutured, flexor surface to flexor surface, dorsal to dorsal, and not flexor to dorsal as it was originally lying. This eradicated the cleft and restored a normal palm.

The second incision was closed, the flexor surface being sutured to the dorsal surface so as to make a slightly improved though still unsatisfactory thumb-index web. The hand was dressed, and adhesive tape was placed circularly about the palm and the index and ring fingers, so as to maintain the normal contour of the palm and to hold the fingers in their proper relation. The thumb was dressed, abducted from the index finger. It was thought wise to defer a plastic operation to restore a normal thumb-index web until a later period.

Second stage, right hand: Two months after the first stage the wounds were well healed. Since the distorted index finger did not move freely, an incision was made along the flexor part of the scar between the index and middle fingers, and the scar and connective tissue was removed from about the tendon of the index finger and along its flexor surface to permit more free extension of the finger. Second stage, left hand: Since there had been some separation of the index and middle fingers, an incision was made along part of the line of the old scar, and new sutures were inserted to hold the proximal phalanges of these fingers in better apposition. The flexor tendon of the index finger that had been found to be inactive at the first operation was dissected free with the hope that some function of this

finger could be restored. The attempt was not satisfactory in that fibrous ankylosis of the interphalangeal joints was found. The finger, however, was straightened as much as the disorientation of the bones of the phalanges would permit. A second incision was made transverse to the web of the thumb and index finger. The scar tissue and the bands of connective tissue of congenital origin holding the thumb in apposition with the index finger were removed. A full thickness free skin graft was then taken from the abdomen and sutured in position to make a new web with wide separation of the thumb and index finger. Sponge pressure was applied to the skin graft. All wounds healed kindly and the skin grew in place.

The result of these various operations was that supernumerary bones were removed, the ring and index fingers brought into apposition, the palm was restored and the fingers placed in normal relation to the palm. The thumb was separated from the hand so as to act in its normal relation to the palm and fingers. The appearance of the hand, fingers and thumb was excellent and the function satisfactory. Unfortunately, the disoriented bones and tendon of the index finger of the left hand impaired the function in this digit. The index finger of the right hand was also disoriented, but had a moderate function. All other digits functioned satisfactorily.

The after-treatment consisted of splinting to maintain the index finger in its proper position during growth and physical therapy to restore and improve function in the thumb and other fingers. An examination three years after the operations disclosed an excellent function which it is believed will improve with the development and use of the hands. The appearance is excellent (see fig. 15).

CASE 31.—*Bilateral medial hypoplasia, syndactylism.*

The patient, a baby, was referred through the courtesy of Dr. Teitelbaum. The right hand was difficult to orientate. There was either an absence of the index finger or its fusion with the thumb, probably the former. The metacarpal of the index finger showed beginning reduplication. There was a wide separation of the thumb from what was apparently a disoriented middle finger. The phalanges were large, and it might be there was fusion of the middle and ring proximal phalanges since the ring finger appeared to be absent although its metacarpal was intact. The little finger was apparently normal.

The left hand showed an intact little finger. All metacarpals were normal. There was complete syndactylism of the middle and ring fingers with distal fusion of the distal phalanges. The thumb and index finger showed syndactylism throughout their length, the bones being separate. The hand presented a wide cleft between the index and middle fingers due to the radial syndactylized group pointing radialward and the ulnar group, ulnarward (fig. 16).

At the time the patient was presented it was deemed wise to defer operative procedures. A poor prognosis was given as to possible results from treatment of the right hand; in the left, however, almost complete functional and cosmetic result should be obtained by plastic procedures.

CASE 30.—*Bilateral medial hypoplasia, syndactylism.*

The patient when first operated on was 2 months of age. At this time the hypoplastic bones were removed and the median cleft repaired. Eighteen months later the syndactylism was treated.

On examination, the right hand presented a loss of the middle finger with a median cleft extending halfway up the palm and moderate syndactylism between the little and ring fingers. Roentgen examination disclosed an absence of the middle finger, a hypoplastic middle metacarpal and apparently overgrowth of the index metacarpal. The left hand presented a similar cleft with absence of the middle finger, complete syndactylism between the thumb and a greatly distorted index finger and moderate syndactylism between the little and ring fingers. Roentgen examination disclosed normal bones of the little and ring fingers. The middle finger was absent, its metacarpal present but bound with the syndactylized radial elements. There was an overgrowth of the proximal phalanx of the index finger due either to a complete fusion of this with the proximal phalanx of the middle finger or to a hypertrophy of this element. The distal phalanx of the index finger was smaller than normal. In both hands the ulnar group was directed ulnarward and the radial group, radialward instead of projecting distalward as in the normal state (fig. 17).

Operation.—First stage, right hand: A transverse incision was made along the cleft extending from the ulnar side of the index finger to the radial side of the

Fig. 16.—Second degree of median hypoplasia of the right and left hands in case 31 (courtesy of Dr. Teitelbaum).

ring finger. The dorsal and palmar flaps were dissected up, and the rudiment of the middle metacarpal removed down to its proximal end. The metacarpal bones of the ring and index fingers were then approximated and held in position by catgut sutures. The connective tissue and skin were then sutured, flexor surface to flexor surface, dorsal to dorsal, and not dorsal to flexor as they had originally lain when incised. The palm and the ring and index fingers were further supported in their new position by circular bands of adhesive tape applied over the dressings. Later experience has shown that we should have sutured the base of the proximal phalanges together to prevent lateral deviation of the digits. This was done at the second stage. First stage, left hand: The repair of the cleft and the removal of the rudimentary metacarpal were carried out in a manner similar to that on the right.

In the second stage of the operative procedures the syndactylisms were destroyed and webs made by lateral flaps from the adjacent fingers, the defects on the sides of the digits being covered by Thiersch grafts; while the result was excellent, later experience has convinced us that in such major syndactylisms as presented in the

left thumb-index digits a bold incision and dissection followed by a full thickness free skin graft is in general followed by more certain good results.

Second stage, right hand: To correct the moderate syndactylism between the fourth and fifth digits, two flaps of skin were raised from the sides of the little and ring fingers respectively, with the pedicles on the dorsum and the two flaps sutured to the flexor surface, making a new web at the proper site. The denuded lateral surfaces of the fingers were covered by Thiersch grafts and pressure sponges applied.

Second stage, left hand: The syndactylism between the fourth and fifth digits was corrected by a similar procedure to that used in the right hand. The syndactylism between the thumb and index finger was corrected by raising a U-shaped flap dissected from the web and the adjacent sides of the digits, the base being on the dorsum. The congenitally contracting connective tissue was removed, the thumb well abducted and the raised flap brought between the digits and sutured on

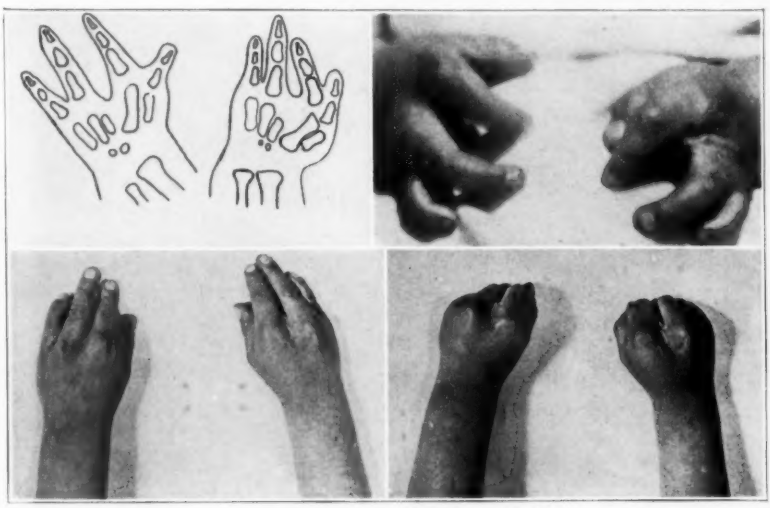

Fig. 17.—Median hypoplasia in case 30. The upper photographs were made before operation; the lower photographs show the result at the end of five years after operation.

the flexor surface. The denuded area left on the digits was covered by Thiersch grafts and pressure sponges applied.

All wounds healed well, and the function of all fingers was excellent. The result after five years may be seen by the accompanying photographs (see fig. 17). At that time the father wrote, "The child does not seem to be handicapped in any manner. He can use a sewing needle, scissors, tools and his handwriting is above normal for a child of four years."

Case 32.—*Right unilateral medial hypoplasia, syndactylism and mongolianism.* Boy B., aged 13, except for the mongolianism, presented no defects other than median hypoplasia and syndactylism of the right hand. The hand had a median cleft extending up to the carpal bones with a complete absence of the middle finger and its metacarpal (fig. 18). There was a moderate syndactylism between the little and ring fingers, both fingers being well formed. The thumb and index finger

were bound in complete syndactylism presenting the appearance of one large digit. The deformity was marked, and the function much impaired. The x-ray pictures (fig. 18) disclosed a complete absence of the middle finger and its metacarpal, normal bones in the ring finger, the two distal phalanges of the little finger present but hypoplastic and the articulations distorted. In the thumb and index finger the metacarpal bones and the proximal phalanx of the index finger were normal, the distal half of the first phalanx and the distal phalanx of the thumb were absent and there were rudiments only of the second and third phalanges of the index

Fig. 18.—Third degree of median hypoplasia in case 32.

finger. The carpal bones were apparently normal. The thumb and index finger were widely separated from the ring and little fingers. At operation the tendons of the index finger and the thumb were found to be in partial fusion; the function of the flexor tendon of the thumb was much impaired, and the tendon going to the index finger was abnormally short.

Operation.—The operative treatment was divided into two stages. At the first stage the thumb and index finger were separated throughout their length, care being exercised to preserve the blood and nerve supply. The partially fused tendons were separated. A full thickness free skin graft from the abdomen was applied to the web and to the denuded lateral surfaces of the two digits extending to the ends

of the digits. A transverse incision was made from the ulnar side of the first phalanx of the ring finger through the cleft to the radial side of the first phalanx of the index finger. Some skin and connective tissue was excised, and the metacarpal bones of the two fingers were sutured together. The proximal ends of the first phalanges were then sutured side to side, and the skin edges were sutured flexor surface to flexor and dorsal to dorsal. Pressure sponges were applied to the large skin graft, and the hand was dressed. The graft healed in place well except for about one-half inch covering the end of the rudimentary index finger. The appearance of the hand was excellent when the patient left the hospital at the end of three weeks, but about a week later there was some separation of the distal ends of the sutured metacarpal bones followed by curvature of the hypoplastic end of the index finger. The thumb tendon failed to give completely satisfactory function, although it was believed that this would improve.

In retrospect, it is believed that we would have been wiser had we transferred the shortened index flexor tendon to the thumb and thus given better function to the newly made thumb. This would have sacrificed function to the distal phalanges of the index finger, but this function in the hypoplastic phalanges was of little importance at best. Moreover the short tendon to the index finger being under tension had tended to produce a separation of the metacarpal heads.

At the second stage the syndactylism between the first phalanges of the little and ring fingers was destroyed by a longitudinal incision of the web, care being taken not to destroy the nerve and blood supply, and a free full thickness skin graft from the abdomen was inserted to cover the defect, after our usual technic. Through an incision along the old scar between the index and middle fingers the heads of the metacarpals and the bases of the proximal phalanges of the index and middle fingers were approximated with sutures, and the hypoplastic, distorted, distal phalanges of the index finger were removed. At the dressing a circular adhesive tape was applied to help hold the metacarpal bones in apposition until healing was complete.

The result of these various operative procedures was that the patient had a much more presentable hand with fair function, although it is believed that a transference of the flexor index tendon to replace that of the thumb would improve the thumb action.

Case 28.—*Medial hypoplasia of left hand; right normal.*

Baby W., who was 13 months of age when she came to the clinic, presented no congenital deformities except in the left hand, which showed absence of the middle and ring fingers with marked contracture of the index and little fingers, which were curved toward each other so that the tips touched. Roentgen examination disclosed a complete absence of the ring finger and a remnant only of the proximal phalanx of the middle finger, with both metacarpals present but distorted. The thumb was normal; the index and little fingers showed all bones present but distorted. Small knobs of tissue were present, representing the middle and ring fingers.

Operation.—An incision was made extending from the middle of the side of the index finger across the web to the side of the little finger. That part crossing the web was of an exaggerated S shape. The two convex parts extended well down on the dorsal and palmar surfaces respectively, so as to make two pedicled flaps one with its base on the dorsum and the other on the palm, the one on the radial side being larger. The remnant of the first phalanx of the middle finger and the head of its metacarpal were removed. The contracting congenital bands were then dissected away from the index and little fingers so that they could be straightened. The radial flap was now sutured to the side of the index finger to cover its exten-

sively denuded surface, and the other flap covered the less denuded surface of the little finger and made a web between the two fingers. Pressure sponges were applied, and the flaps healed in position. The result gave excellent function, although the absence of the two fingers permitted some lateral deviation of the fingers to recur.

CASE 24.—*Left medial hypoplasia and syndactylism; clinodactylism.*

Baby H., aged 4 years, was born with syndactylism of the four fingers, clinodactylism with hypoplasia of the middle phalanx of the little finger and hypoplasia of the index, middle and ring fingers. The thumb and all metacarpal bones were present. There was a rudiment consisting of about one half of the proximal phalanx of the index finger, a similar amount of the first phalanx and a rudiment of the middle phalanx of the middle finger, and a fairly well developed proximal phalanx and a small rudiment of the second phalanx of the ring finger (fig. 19).

At a previous operation elsewhere the little finger had been separated from the ring finger. At our clinic the three middle fingers were separated by longitudinal incisions, and free full thickness skin grafts were applied after the manner described in the section dealing with syndactylism. The functional and cosmetic results were satisfactory.

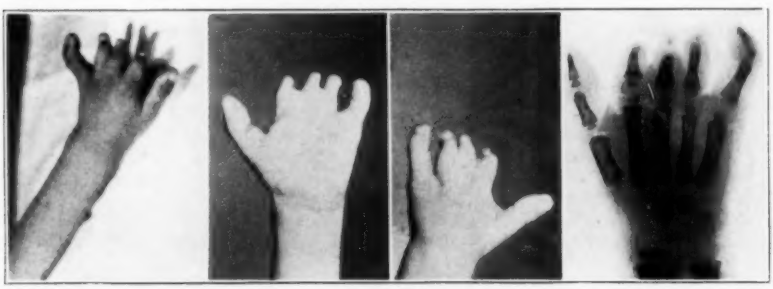

Fig. 19.—Median hypoplasia clinodactylism in case 24.

CASE 35.—*Medial hypoplasia, left hand.*

This patient, presented through the courtesy of Dr. Goldstine, had a complete cleft of the left hand extending to the wrist with two digits present, apparently the first and fifth. The function was excellent. The bones of the thumb as well as the metacarpal showed hypertrophy. The metacarpal of the little finger was intact, but there were only two phalanges, the distal appearing as a normal phalanx. It was impossible to say whether the first and second phalanges were fused or that one had been lost. Two small rudiments of medial metacarpals were present, believed to be from the third and fourth metacarpals (fig. 20 *A*).

The function of the hand was so good that operative treatment was not advised.

CASE 36.—*Medial hypoplasia, left hand; absence of pectoralis major, left; hypoplasia of pectoralis minor, left; symphalangism.*

The patient, aged 24 years, presented a history showing hereditary tendency. She had excellent use of the deformed hand, and grasped well between the two digits (fig. 20 *B*).

The hand consisted of two digits, one a radial (thumb) and one an ulnar (little finger). The radial digit carried no nail, and there was apparently a loss of the distal phalanx. The metacarpophalangeal joint showed excellent function, but the carpometacarpal joint was lax and the metacarpal slipped radially and dorsally on use. The carpometacarpal joint of the little finger was intact and function was

excellent. The phalanges were fused at the joints, and the head of the fused finger lay anterior to the head of its metacarpal although flexion was present and a gliding motion in the transverse and vertical axis was permitted. Rudiments of the metacarpals of the second, third and fourth digits were present where small nodules the size of a pea were seen.

Owing to the excellent function of the hand, no operative procedures were advised.

The extreme type of medial hypoplasia is reported by Seroiczkowski.[9] The patient presented a bilateral median hypoplasia with one carpal cartilage and two small rudiments, representing a single bone of the thumb and little finger, respectively. The hands were similar, and both feet presented an almost identical picture. A more extreme similar lesion with loss of the radial hand and ulnar hypoplasia is reported by

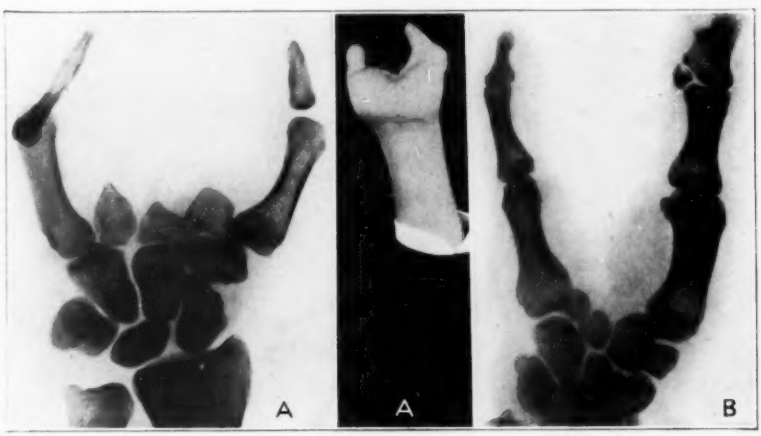

Fig. 20.—Roentgenogram and photograph (*A, A*) showing median hypoplasia, fourth degree, in case 36. (Courtesy of Dr. Goldstein.) Roentgenogram (*B*) showing atypical hypoplasia in case 35. There is no certainty as to absent digits.

Jaroschy in which the radius and ulna of the left forearm are widely separated at the distal ends (fig. 21).

These varying clinical pictures are seen to present varying degrees of medial hypoplasia with the remaining ulnar and radial elements pointing laterally instead of distalward. At times the middle finger only or the middle finger with its metacarpal is involved. In others, the middle and ring fingers, or the middle, ring and index fingers, or the middle, ring and little fingers with a lesser degree of hypoplasia of the thumb and index fingers are found involved with varying degrees of loss of the metacarpal and carpal bones. We often find hypoplasia of

9. Seroiczkowski, A.: Symmetrical Malformation (Cleft) of Hands and Feet, Ztschr. f. d. ges. Anat. **89**:145, 1929.

a digit and disorientation of its remaining elements. This disorientation frequently is expressed by a transversely lying proximal phalanx or metacarpal. These cross-lying bones seem to bridge the defect, and they may articulate with adjacent articulations, e. g., a transversely lying metacarpal with the articulation of an adjacent metacarpal and its phalanx, or a cross-lying phalanx with adjacent and interphalangeal articulation. To our mind, unjustifiably, Lewis and Embleton dignify these variations with descriptions as distinct types. We believe them to be but an expression of varying degrees of disorientation and not clinical entities. The adjacent bones may show hypertrophy, and the question arises whether this is a simple hypertrophy or an enlargement due to fusion of two elements. The lateral disorientation is con-

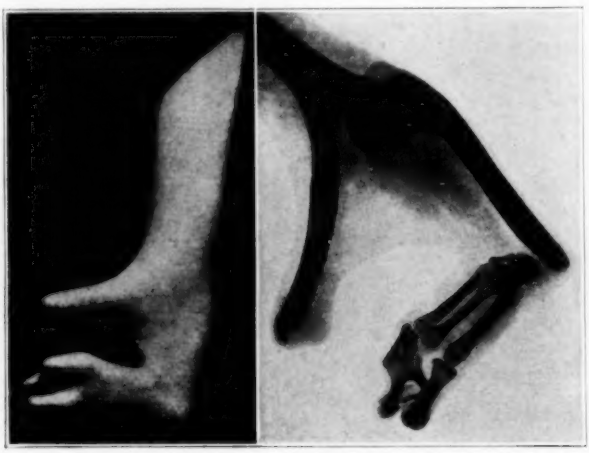

Fig. 21.—Excessive separation of the ulnar and radial elements with loss of the medial and radial digits, metacarpals and carpals. (From Jaroschy: Arch. f. orthop. **25**:482, 1927.)

spicuously present and is most frequently expressed by moderate hypoplasia of various bone or muscle elements and syndactylism, especially on the ulnar side. Kummel reported that in 17 patients there were 7 hands with radial syndactylism alone, 21 with ulnar and 3 with both ulnar and radial. In our observations bilateral syndactylism of the involved hand is more commonly present. Polydactylism is less often present. At times we find a rudimentary extra digit at the end of a phalanx.

Associated lesions are not uncommon, e. g., deformity of the lower end of the radius, absence of the pectoralis major or minor and various other lesions. Very frequently we find involvement of the feet and a similar lesion. In 59 persons, Perthes found one hand involved in 11 cases,

both hands in 5, both feet in 9, both feet and one hand in 4, both hands and both feet in 30. In 48 of the 59 patients more than one extremity was involved.

Spurious split hand may be produced by lack of differentiation of metacarpal bones. This is illustrated by the patient presented by Bircher [10] (fig. 22).

Treatment: Much can be done for the simpler types of median hypoplasia. The treatment consists of surgical restoration followed by splinting and physical therapy. The purpose of the surgical treatment is the restoration of the fingers and tendons to the position of function and cosmetic effect. Function depends on the position of the fingers

Fig. 22.—Spurious lobster-claw hand. (From Bircher: Beitr. z. klin. Chir. **121**:187, 1918.)

and the degree of disorientation of the muscles, nerves, tendons and joints remaining. The fingers can be placed in a relatively normal position, the function of the joints may be improved and tendons may be transplanted, but we know of little that can be done for impaired function of the intrinsic muscles and nerves except use and physical therapy. Fortunately, nature in time does much for these, and the hand, while not functioning after the usual pattern, still develops a function of its own that serves almost all purposes. This is due to the development of the intrinsic muscles working in their own peculiar way and to the fact that the fingers are moved by the forearm muscles which are little involved.

10. Bircher, E.: Die Gabelhand, zugleich ein Beitrag zur Theorie der Miss-Bildungen, Beitr. z. klin. Chir. **111**:187, 1918.

Operative Treatment: This may be divided under four heads: (1) restoration of the proper position of the fingers, (2) treatment of the associated tendons, (3) treatment of the associated joints and (4) treatment of the syndactylism and polydactylism.

These procedures are generally so extensive as to demand that the operation be divided into two and sometimes three stages. The work done in these stages naturally varies with the conditions. Generally, at the first stage the fingers are restored to their correct position and such other work as may be advisable is carried out, and at the second the syndactylism is treated.

When the cleft extends into the palm the primary incision generally lies transversely along the web, reaching halfway up on the proximal phalanges of the separated intact fingers. This simple incision is especially advised when there is more or less cleft of the palm. When the palm is intact it may be advisable to carry the transverse incision of the web around the base of the proximal phalanx of the index finger. In the first instance the purpose is to permit restoration of the palm when the fingers are approximated. In the second the purpose is to permit transference of the index finger to lie adjacent to the ring finger. This avoids sacrifice of skin which is used to make a web between the thumb and index finger. Special conditions will demand variations of these incisions.

In the first type of operation the incision of the skin having been made, it is dissected free from the underlying tissue and all transverse-lying or disoriented bones removed, care being used not to destroy nerve and vascular tissue (fig. 23). A deep dissection is then made of the metacarpal of the affected finger, and this is removed down to its base. This leaves a defect and permits us to approximate the lateral-lying metacarpals. Care should be exercised to see that the sutures bringing these together are passed through firm tissue since there is a tendency for the bones to separate. We, therefore, use heavy chromic catgut and pass two or three sutures, attempting to bring the heads of the metacarpals in close apposition. The fingers also have a tendency to lateral deviation and the joint surfaces have grown in the distorted position so that it is necessary to pass one or two sutures through the tissue at the proximal end of the proximal phalanges to hold them in close apposition. The skin and subcutaneous tissue are now sutured. The subcutaneous tissue on the palm is so sutured as to leave an elevation rather than a longitudinal depression in the palm. The skin is sutured, flexor surface to flexor surface and dorsal to dorsal, not flexor to dorsal as originally found. In the dressing, circular strips of adhesive plaster encircle the dressed palm and fingers so as to support the suture of the bones. This should be maintained for three weeks at least since there is a marked tendency for them to separate.

If the palm is intact and there is not a marked syndactylism of the index finger and thumb, the radial end of the transverse incision of the web passes around the base of the proximal phalanx of the index finger. This permits us to dissect away the skin without impairing the blood supply, the intervening bones having been removed as previously

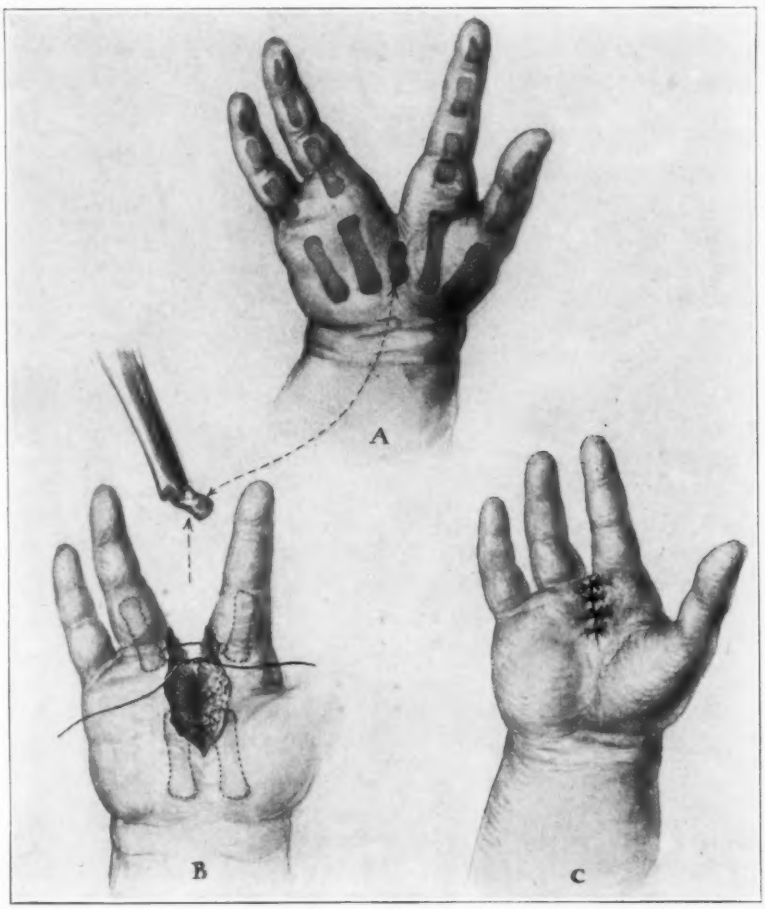

Fig. 23.—Technic of union of the ulnar and radial elements in lobster-claw hand.

described; to transfer the dissected index finger over to its prepared bed beside the ring finger, and to use the skin thus left on the radial side of the index finger for a web between the index finger and the thumb (see fig. 24 and case 29). The dressing and associated procedures are as previously described. This operation has not been used in cases in which there is extensive syndactylism between the index finger and the thumb since it is feared that the extensive dissection

necessary followed by skin grafting to cover the defect might impair the blood supply of the index finger, especially since sponge pressure is used in the after-dressing of the free skin grafts. Manifestly, varying conditions may demand modifications of these two typical procedures that have been used most frequently.

Generally, no operative treatment on the tendons is necessary since if they are disoriented the associated finger is also useless. At times, however, a tendon may be found in the same synovial sheath with an adjoining tendon, or it may be fused or absent. If in the synovial

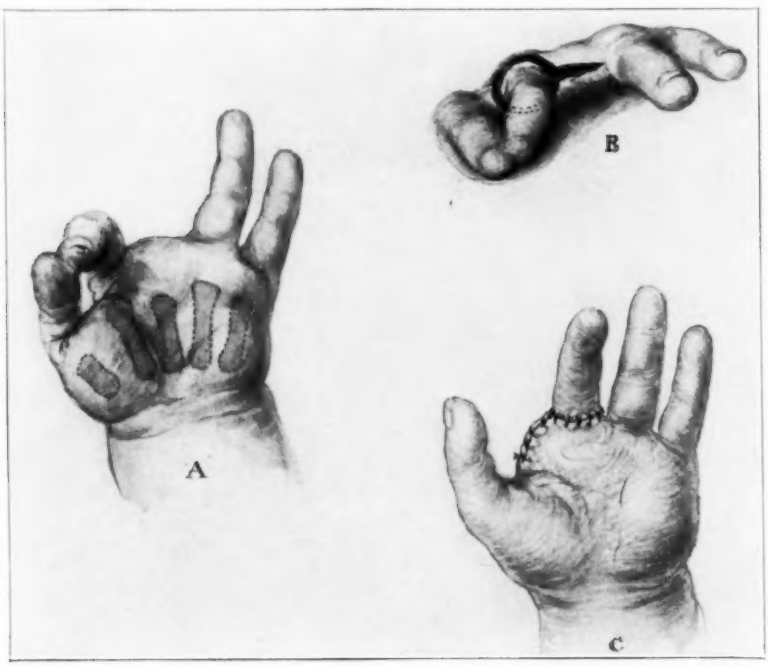

Fig. 24.—Technic of sliding operation for the index finger in certain types of lobster-claw hand.

sheath of an adjoining tendon, it may be removed from the common sheath and placed with its proper finger, or a good tendon of a distorted finger may be transferred to take the place of a poor tendon. This latter step is most frequently demanded if we wish to restore function to the thumb, which is very important. The index tendon may then be used if the index finger is hypoplastic, but if this finger is functioning, a tendon may be transferred later from the foot.

At times symphalangism may be present, and it may seem advisable to treat the condition at the time of the primary operation or later, especially if the bones are distorted. More frequently, however, it is neces-

sary to repair a joint because of a distorted relation of the joint surfaces or because a transversely lying metacarpal or phalanx that had joined with the bones of the adjacent finger, making a common articulation, had been removed. At other times it will be found advisible to remove hypoplastic bones from fingers which we are preserving either for cosmetic or functional purposes. This applies to the distal phalanges most commonly.

The repair of the joints is not infrequently associated with the removal of congenital contracting bands which hold the distal phalanges in a distorted position, e. g., clinodactylism.

The treatment for syndactylism is the same as that discussed in the section dealing with that subject. Ordinarily, since the syndactylism involves the thumb and index finger and the little and ring fingers, the treatment is carried out in two stages, since we fear that an operation involving both sides of the index and ring fingers at the same time might impair their vitality either by the necessary dissection or the subsequent sponge pressure used on the skin graft.

When the hand is restored to as nearly normal relation as possible, we may find it advisable to institute physical therapy to stretch tendons, destroy contractions and develop muscles. We also have at times made tension splints to supplement these procedures, the splints being designed on the principles described elsewhere in the discussion on that subject. Again we have made a detachable aluminum finger splint designed to hold a distorted finger in position so that newly made joints or distorted bones may grow in a proper relation. These are made after the type of the Lewin splint used in the treatment for ruptured extensor tendons of the distal phalanges.

The results obtained in our experience are often surprisingly good, especially after a few years of use of the restored hand. Cosmetically, the absence of the middle finger is hardly noticed; functionally, the hand may be almost perfect (see case 30, fig. 17).

(To be Concluded)

MONARTICULAR ARTHRITIS SIMULATING TUBERCULOSIS

A CLINICAL AND PATHOLOGIC STUDY OF TWENTY-FOUR CASES

ALAN DeFOREST SMITH, M.D.
NEW YORK

The common occurrence of a type of monarticular arthritis that frequently simulates tuberculosis very closely is indicated by a study of a series of cases in which the patients were treated at the New York Orthopaedic Dispensary and Hospital and the results of which are presented in this paper. Few references to the condition appear in the literature. Friedrich [1] and Spitzy [2] mentioned that monarticular arthritis may be mistaken for tuberculosis and that the differential diagnosis is often difficult. A conviction, which has become more firmly established with added experience, that in many instances of chronic diseases of the joints a diagnosis cannot be made without exploratory operation, biopsy and tests on guinea-pigs [3] has led to the discovery of this group of cases, which presents a number of interesting features.

From March, 1924, to January, 1930, twenty-four patients with such cases were operated on in the New York Orthopaedic Hospital. In each case the chief purpose in operating was to establish a diagnosis. A careful tissue examination was made in all cases, and, with two exceptions, a guinea-pig test was done. The presence of tuberculosis was excluded in each instance. The joints involved were: the knee, in eighteen cases; the hip, in four; the elbow, in one, and the tarsus, in one. The ages of the patients at the time of operation varied from 19 months to 35 years, the average being 14½ years. Fourteen patients were females and ten males. After consideration of all the available data, including a careful history and physical examination, roentgenograms, blood counts and tuberculin tests, the diagnosis in the twenty-

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From the clinic of the New York Orthopaedic Dispensary and Hospital.

1. Friedrich, H.: Unspezifische Gelenkentzündungen unter dem vollen klinischen Bild der Tuberkulose (Scheinbare Tuberkulosen, Pseudotuberkulosen), Mürchen. med. Wchnschr. **75**:1153 (July 6) 1928.

2. Spitzy, H.: Zur Diagnostik der Knochen und Gelenktuberkulose, Med. Klin. **17**:1 (Jan. 6) 1921.

3. Smith, A. DeF.: The Early Diagnosis of Joint Tuberculosis, J. A. M. A. **83**:1569 (Nov. 15) 1924.

four cases before operation was: synovitis (probably tuberculous) in ten, tuberculosis (without qualification) in ten, chronic or subacute arthritis in two and internal derangement in two. It is thus seen that in the majority of cases the diagnosis was wrong, and that the condition with which it most frequently was confused was tuberculosis, in twenty of twenty-four cases. The duration of the symptoms, which varied from a few months to as many as ten years, with involvement of only one joint, was suggestive of tuberculosis. In one case, the presence of a chronic pulmonary infection, which at first was believed to be tuberculosis but which afterward was diagnosed as streptococcus infection, suggested that the process in the knee also was tuberculous. In two of the patients an injury to the knee, followed by swelling, limitation of motion and tenderness over the medial meniscus, prompted the diagnosis of injury to that structure.

The physical examination in practically all of the cases revealed the classic signs of tuberculosis of the joints, namely, swelling with little tenderness or heat, limitation of motion from muscle spasm and atrophy of the adjacent muscles. There can be no question that these signs are just as common in any other chronic inflammation of a joint as in tuberculosis, and that they can be given no great weight in making a diagnosis. It was interesting to find that in nine of these patients, all of them children with involvement of the knee joint, the affected leg was from ¼ to 1 inch (0.64 to 2.5 cm.) longer than the normal one. This had been noted previously in cases of tuberculosis of the knee joint, and it evidently is caused by an increased blood supply and stimulation of growth at the epiphyseal cartilages. It was seen in the roentgenograms taken in these cases that the epiphyses of the femora and tibiae, as well as the patellae, were thicker than on the normal side.

Study of the roentgenograms of the twenty-four patients, in comparison with those of a series of proved cases of tuberculosis of the joints, shows that they have very little positive value in making the diagnosis. A definite diagnosis of arthritis was made from the roentgenograms in three cases, and two were thought to show nothing abnormal. The findings in the remainder were: effusion in the joint, thickening of the synovial membrane, thin joint space and decalcification of the bones. These are all found in synovial tuberculosis and therefore are valueless from the standpoint of differential diagnosis. The roentgen reports in five cases stated that the findings were consistent with, or suggested, tuberculosis.

The tuberculin test was positive in nine cases, doubtfully positive in three and negative in eight. In several of the earlier cases the Pirquet technic was used, but in the majority the Mantoux test was performed. In all cases in which a negative result was obtained, the test was repeated at least once. It would seem that a repeatedly nega-

tive intradermal test with both human and bovine tuberculin in a patient in good general condition is important and should be given much weight in making a diagnosis. Baldwin stated, however, that he would not exclude the possibility of an old tuberculous lesion, which may recently have become active, because of a negative Mantoux test.[4]

Fig. 1.—A section of a villus, showing round cell infiltration and dilatation of the blood vessels.

Previous experience with the quantitative test for the purpose of provoking a general and focal reaction had shown that it was of no value, for which reason it was not used in any of these cases.[3] The Wasser-

4. Baldwin, Edward R. (Director of Trudeau Sanitarium): Personal communication to the author, Jan. 1, 1931.

mann or Kahn reactions were negative in the nineteen cases in which the tests were done.

The blood count was not particularly helpful in the diagnosis, although the average leukocyte count was higher than that in the normal or the tuberculous patient. There were fifteen counts above 8,000,

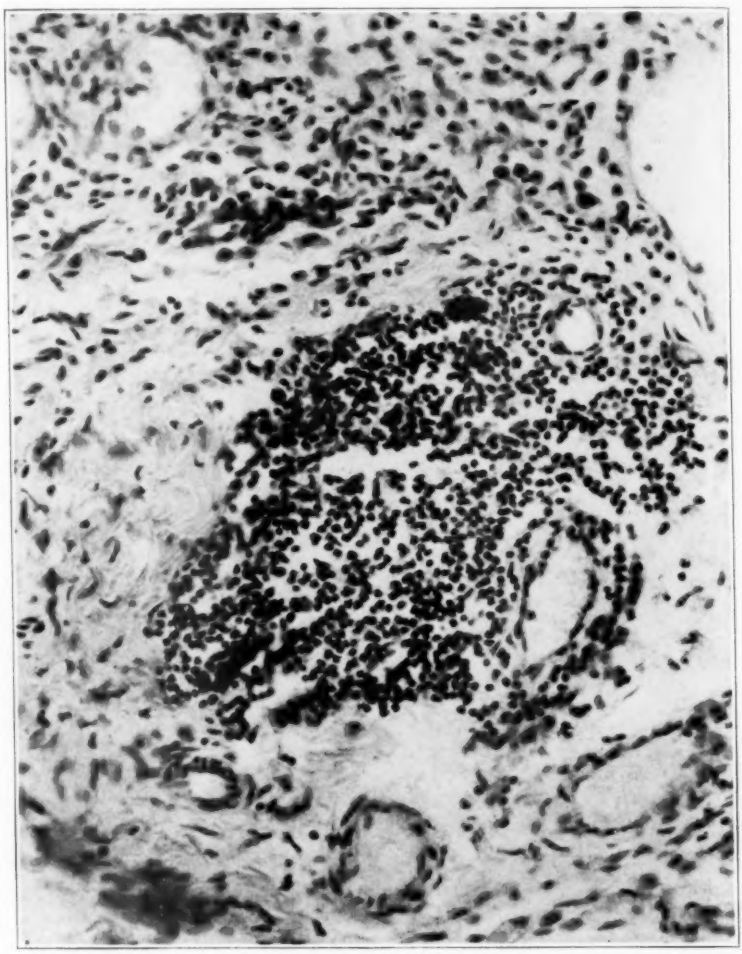

Fig. 2.—Higher magnification of an area from figure 1, illustrating clumping of the round cells about the blood vessels.

and only four of 8,000 or less. One patient whose condition was diagnosed as arthritis before operation had 19,500 leukocytes. The mononuclear cells were more than 30 per cent in twelve cases and less than 30 in six. The important point in this connection is that the blood count cannot be conclusive, and that it seldom is even suggestive.

Two knee joints were aspirated before operation, and the fluid was injected into guinea-pigs, with negative results. This procedure is no longer used generally, because the result cannot be learned for six weeks, because it is inconclusive when negative, and because it has been found that if tuberculosis is present, it usually can be discovered by immediate section of the tissue at the time of operation.

The operation in each case was done primarily as an exploration. One medial meniscus was removed because it was frayed, and three synovectomies were performed, including the case in which the cartilage was removed. Synovectomy was done subsequently in a fourth case in which symptoms recurred after four years. The incision used in every case was a median longitudinal one, parallel to the patella. By extending this upward a short distance above the patella, an excellent exposure can be had, and even the lateral portion of the joint can be seen fairly well. In several instances, a lateral incision also was made.

The appearance of the joints at operation is of special interest. In twenty-one cases the synovial membrane was greatly hypertrophied and tended to bulge out as soon as the capsule was divided. It was edematous and congested and varied in color from dark red to pale, dirty gray. In several cases it was almost gelatinous in appearance. The fluid in most cases was more abundant than in normal joints and usually was clear yellow. In a few instances coagulated lymph or fibrin was found in the joint. In the knee joints a pannus of varying size regularly was found growing over the margins of the articular cartilage of the femur. This conforms exactly to the picture seen in many cases of synovial tuberculosis.[5] It commonly was found that the thickened synovial membrane separated easily from the capsule, and that there was a distinct line of cleavage. Fibrosis with adhesions, but no suggestion of active disease, was found in two knees. The articular cartilage was well preserved in all except one knee, in which it was somewhat fibrillated.

Lipping at the margins of the joint caused the operator in two cases to decide from the gross appearance that he was dealing with chronic arthritis. Although the surgeon in each case had seen many tuberculous joints, he had the impression in sixteen cases that the lesion very probably was tuberculous, and in four others he was in doubt about its nature.[6] This again emphasizes the fact that no matter how

5. Smith, A. DeF.: The Pathology of Joint Tuberculosis in Its Earlier Stages, Arch. Surg. **12**:740 (March) 1926.

6. Twelve patients were operated on by me and the remainder by three other members of the staff.

experienced a surgeon may be in such work, he usually cannot determine by the appearance of a joint alone what the nature of the lesion may be.

The picture presented in the sections of tissue from these joints varied from that of an acute to that of a chronic inflammatory process.

Fig. 3.—Diffuse infiltration of mononuclear cells. There is no thickening of the synovial layer.

In the large majority, there were hypertrophy of the villi, thickening of the surface layer of synovial cells and, underlying this, a greatly thickened subsynovial tissue. An exudate often was present on the surface. In nearly all cases there was some edema, and in a few this feature was very striking. The blood vessels were numerous and

dilated. The prevailing type of cell infiltrating the tissue was the small mononuclear, but in a few cases there also were numerous plasma cells. The lymphocytes were scattered diffusely through the tissue, but also were found in dense spherical clumps that bore no resemblance to tubercles. In six cases the round cells were massed about the blood

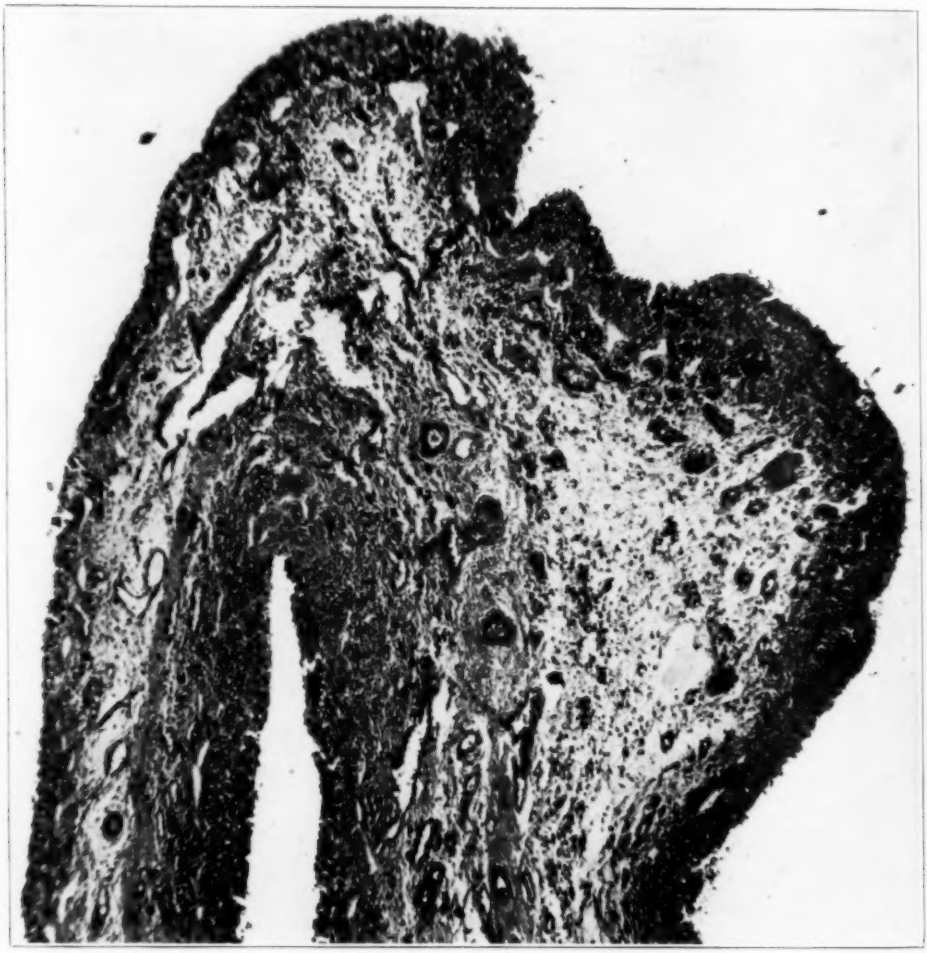

Fig. 4.—A thick synovial layer. There is an infiltration of cells immediately below the surface.

vessels in a manner that is said to be characteristic of syphilis, and indeed, the pathologist thought that there was a strong probability that these might be cases of syphilis. In all, however, the Wassermann reaction was negative, and there was nothing in the history or physical examination to corroborate this diagnosis. Obliterating endarteritis

was noted in one case. Polymorphonuclear cells were present in some cases, but were not numerous. Areas of necrosis and cloudy swelling of the adjacent regions were found in two examinations. The predominant feature of one case was well organized fibrous tissue with little infiltration of cells.

There is a record of cultures in seventeen cases. One resulted in a growth of Staphylococcus aureus. The onset of symptoms had been sudden, ten weeks previously, and while it was thought at operation

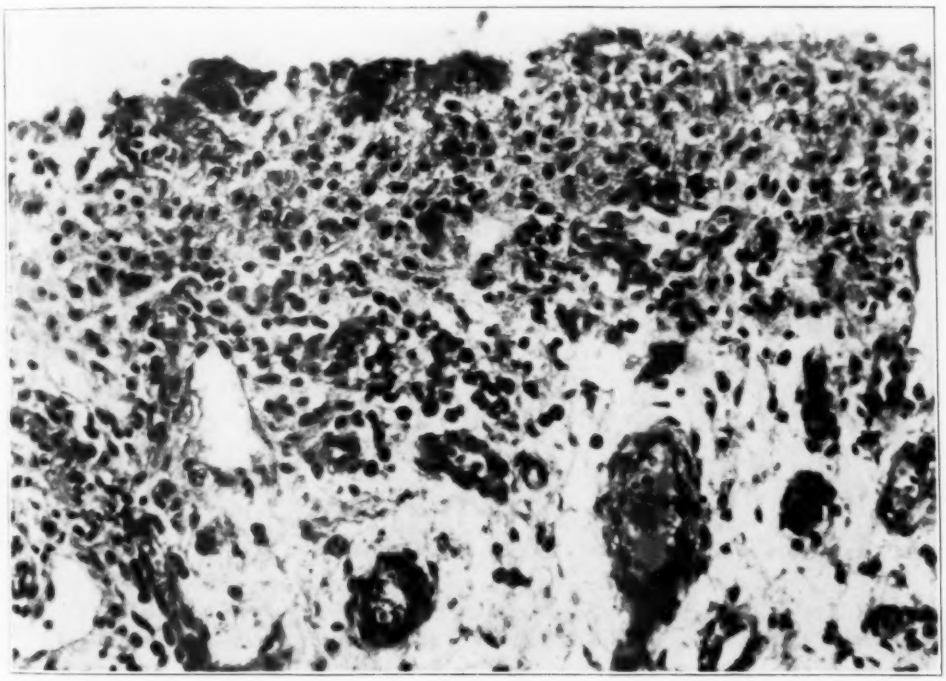

Fig. 5.—A small area of the section shown in figure 4, under higher magnification.

that the appearance was that of tuberculosis, there had been little doubt that the case was one of subacute arthritis. Culture in another case showed a growth of Staphylococcus albus and a gram-positive bacillus, which were considered contaminants. The others were all negative. In a great majority of cases, the tissue, as well as the fluid, was cultured on ordinary mediums, including agar slants and dextrose broth. It is certain that no results are to be expected in these cases except by special bacteriologic technic, and it is questionable whether organisms can be recovered from such joints at the stage when these operations

were done, although Cecil[7] recently reported growing streptococci in cultures from cases of arthritis. Tests on guinea-pigs with fluid or tissue, and often both, were done in twenty-two cases. The results in all were negative.

The behavior of these joints after exploratory operation was studied. One patient with arthritis of a hip subsequently developed symptoms in several joints and was treated with vaccines. He died of pneumonia thirteen months after operation. Four other patients later had symptoms in other joints, which would have simplified the diagnosis had they occurred earlier. A hip joint in which the bone of the femoral head and acetabulum both were affected became more and more stiff and painful until it finally was necessary to do an arthroplasty. A child whose symptoms and physical signs promptly disappeared after exploratory operation had no further trouble until marked swelling and effusion in the knee occurred four years later. A second operation was performed, revealing a greatly hypertrophied, congested, synovial membrane, which was excised. Swelling then disappeared, and a normal range of motion was obtained. An adult who was found to have a markedly hypertrophied, chronically inflamed, synovial membrane of the left knee was advised to have a synovectomy but refused. When last examined, his knee was still swollen and stiff. Of the remaining sixteen patients, fourteen have little or no stiffness, swelling or disturbance of function. In two the end-results are unknown.

REPORT OF CASES

The following two cases present typical histories:

CASE 1.—E. B., a girl, aged 3½ years, was first seen in the outpatient department of the New York Orthopaedic Dispensary and Hospital on Aug. 12, 1922. Her left knee became swollen and stiff and she began to limp following a fall from a chair in December, 1921. She was a well developed and nourished child who walked with a limp, owing to limitation of motion in the left knee. Physical examination gave negative results, except for the left lower extremity. The left knee was moderately swollen, and the patella floated. The thigh and calf were slightly atrophied. The temperature of the joint was slightly elevated. The leg could be extended to 180 degrees, but flexion was limited at 75 degrees by muscle spasm. Roentgen examination showed slight decalcification of the bones of the knee joint and effusion in the joint. On August 28, the joint was aspirated, and 15 cc. of blood-tinged fluid was obtained. This was cultured and injected into a guinea-pig. Culture was negative, and the guinea-pig failed to develop tuberculosis. In November, the physical signs persisted, and it was felt that in spite of the negative laboratory tests the joint probably was tuberculous. The parents were urged

7. Cecil, Russell L.; Nichols, Edith E., and Stainsby, W. J.: Bacteriology of Blood and Joints in Chronic Infectious Arthritis, Arch. Int. Med. **43**:571 (May) 1929.

to allow the patient to go to the country branch of the New York Orthopaedic Hospital, but refused. A brace was applied. In June, 1924, there was atrophy of the thigh and calf, and the knee was slightly swollen. Motion was limited from 160 to 180 degrees. Roentgen examination showed general decalcification of the bones and enlargement of the patella and epiphyses. The brace was gradually discarded in September, 1924. In November, the Wassermann reaction was negative, as were Pirquet tests with both human and bovine tuberculin. Examination of the blood showed 4,480,000 red cells, 6,800 white cells and 52 per cent polymorphonuclears. In July, 1926, the patient injured the knee, and it became slightly more swollen. Slight crepitus was present, and flexion was limited to 80 degrees. Roentgen examination showed decalcification of the bones and synovial thickening without evidence of fluid. The Wassermann and Pirquet tests were repeated and gave negative results. By aspiration, 4 cc. of blood-tinged fluid was obtained. Cultures and tests on guinea-pigs gave negative results.

An exploratory operation was performed on the left knee on Oct. 5, 1926. The synovial membrane was hypertrophied and congested. A pannus extended over the medial condyle of the femur, but the bone and cartilage were not involved. Tissue was removed for section, culture and tests on guinea-pigs and the incision was closed. The incision healed by primary union. Early active and passive motion was begun, and convalescence was uneventful. Culture of this tissue was negative. Sections showed very marked, diffuse, round cell infiltration with numerous dilated blood vessels. On April 1, 1930, there was no swelling, limitation of motion or disturbance of function of the left knee. The left lower extremity was ¼ inch (0.64 cm.) longer than the right.

Case 2.—E. B., a man, aged 28, was admitted to the outpatient department of the New York Orthopaedic Hospital on Oct. 16, 1928. Two years previously he began to have swelling and stiffness in his left knee. There was no history of injury. Symptoms were intermittent, but the swelling never completely disappeared. No other joints were involved. Baking and diathermy were used, and plaster casts were applied twice. Recently he had been advised by another surgeon to have his knee operated on for removal of cartilage and "scraping of the bone." There was no history of pulmonary tuberculosis. The patient was a short, fairly well developed and nourished man. The tonsils were large and appeared infected. The teeth were in good condition. Physical examination otherwise gave negative results, except for the left lower extremity. The left knee was swollen and slightly warmer than the right. The patella floated. Motion was limited from 100 to 160 degrees by muscle spasm. There were 1 inch (2.5 cm.) atrophy of the thigh and ¾ inch (1.87 cm.) atrophy of the calf, and the circumference of the knee was 1¼ inches (3.14 cm.) greater than the right. Roentgenograms of the left knee showed a slight, dense, irregularly distributed effusion and a thin joint space, moderate decalcification and slight productive reaction, consistent with long-standing avirulent tuberculosis. Roentgen examination of the chest showed sclerotic nodes and moderate peribronchial infiltration, suggesting tuberculosis. The Mantoux test, with 0.05 mg. of tuberculin, was negative. The test was repeated, with 0.1 mg., with a strongly positive result. The Wassermann reaction was negative. Examination of the blood showed: white cells, 8,000; polymorphonuclears, 65 per cent; lymphocytes, 35 per cent.

The patient was sent to another hospital for removal of his tonsils. Examination of the tonsils gave negative results for tuberculosis. The patient was admitted to the New York Orthopaedic Hospital on Nov. 5, 1928, and an exploratory operation was done on November 9. The joint was exposed on the medial side. The

synovial membrane was thick, grayish and very soft and friable. The cartilage on the medial side of the femur was not eroded. A quantity of turbid fluid containing flakes of fibrin escaped. Pieces of synovial membrane were removed and were examined immediately by frozen section. The report was chronic inflammation, and the incision was closed, although it was believed from the appearance of the joint that the condition was tuberculosis. The sutures were removed in nine days, and the incision was healed. There was slight effusion, and motion was from 35 to 170 degrees. The patient was discharged on the eleventh day to await the guinea-pig test and further examination of the tissues. A culture of the fluid was sterile, and guinea-pigs inoculated with the fluid and tissue failed to develop tuberculosis. Permanent sections of the tissue showed immense numbers of blood vessels, some of which seemed to show thickening of the wall. There was a lymphocytic and plasma cell infiltration, occurring for the most part around the blood vessels, but seen in one or two areas as dense rounded masses. No necrosis or tubercle formation was seen. The diagnosis was changed to chronic arthritis of the left knee, and the patient was advised to have a synovectomy, but refused. When last seen, on Feb. 12, 1929, he still had swelling and limitation of motion of the knee.

CONCLUSIONS

1. Monarticular arthritis, which may simulate tuberculosis very closely, is not uncommon.

2. It is impossible to differentiate these lesions from those of tuberculosis by physical examination or the x-rays.

3. A repeatedly negative Mantoux test in such a case is suggestive but not conclusive.

4. Exploratory operation often is the only means of making the diagnosis, and even then the gross appearance of the joint is not to be relied on.

5. The histologic picture is that of a chronic inflammation. Cultures on ordinary mediums are negative.

6. The majority of the patients recover without further treatment.

PRIMARY CARCINOMA OF THE GALLBLADDER

REPORT OF NINETEEN CASES *

HAROLD J. SHELLEY, M.D.
NEW YORK
AND
LLOYD I. ROSS, M.D.
CLEVELAND

The subject of primary carcinoma of the gallbladder may be considered to be of interest more from an academic than a clinical point of view. This statement is made because the disease is such that a preoperative diagnosis sufficiently early for successful surgical measures is practically impossible. Those few cases that have been reported in which cure was obtained are almost without exception those in which the carcinoma was found during an operation for some other condition, particularly gallstones. Even the greater majority of these were not diagnosed macroscopically but in the routine microscopic examination of gallbladders removed because of cholecystitis or cholelithiasis. In the only case among the 19 here reported in which the patient is still living, the carcinoma was not suspected during the operation but was found in the course of routine pathologic examination. The patient is still living and well six and one-half years after cholecystectomy which was done for cholecystitis and cholelithiasis.

Isolated cases of this disease were reported by de Stoll [1] in 1771, Hallé [2] in 1786 and Baillie [3] in 1793. However, the description by the latter coincided more nearly with the picture of tuberculosis. Frerichs [4] described the disease in 1858. Villard,[5] in 1869, collected 17 cases. Musser [6] collected 100 cases from the literature to 1889. From that date on, the cases reported become much more frequent. For other series of collected cases see the discussion of the relation between gallstones and carcinoma of the gallbladder.

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* These nineteen cases comprise the total number found at operation and proved microscopically from 1916 to 1930 inclusive, at St. Luke's Hospital, New York.

1. de Stoll, quoted by Rolleston and McNee: Diseases of the Liver, Gallbladder and Bile Ducts, London, The Macmillan Company, 1929, p. 691.

2. Hallé: Hist. Soc. de méd., Paris, 1786, p. 125.

3. Baillie, M.: Morbid Anatomy, London, J. Johnson, 1793, p. 158.

4. Frerichs, F. T.: Diseases of the Liver, translated by the New Sydenham Society, London, 1861, vol. 2, p. 479.

5. Villard: Bull. Soc. anat. de Paris **44**:217, 1869.

6. Musser, J. H.: Boston M. & S. J. **121**:528, 1889.

INCIDENCE

Sex Incidence.—Rolleston and McNee [7] reported that from the Registrar General's returns in England and Wales from 1913 to 1920 there were 2,296 females and 946 males who died from malignant disease of the gallbladder, an incidence of 2.4:1. Ewing [8] calculated the relative incidence as 4 or 5:1; Schröder [9] as 5:1; Kaufmann,[10] Harley,[11] Kraus [12] and Colwell [13] as 2:1. Thirteen of our 19 cases were in females and 6 in males, an incidence just over 2:1. These figures correspond closely to the various estimates made as to the relative frequency of occurrence of gallstones in the two sexes.

Age Incidence.—Ewing [8] stated that carcinoma of the gallbladder occurs nearly always after the age of 40 and gave 58 years as the average age occurrence in both sexes. In our list the average age is 60.7, the youngest patient being 48 and the oldest 70. Moxon [14] reported a case of villous carcinoma of the gallbladder in a child 4 years of age. Proescher [15] reported a case in a man 22 years old. Kaufmann,[10] Haas [16] and Chavannaz [17] each reported a case in a patient 25 years of age. Thomas and Noica [18] reported a case in a patient 90 years old. Kaufmann [10] mentioned a woman, aged 95, who had carcinoma of the neck of the gallbladder with a stone. Haberfeld [19] stated that the oldest patient he found was a man, aged 93, whose case was reported by Riedel.[20]

Incidence in Relation to Gallstones.—This subject will be discussed fully in the discussion of etiology.

General.—Carcinoma of the gallbladder is usually given fifth place in frequency of incidence among the organs concerned with digestion.

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7. Rolleston and McNee: Diseases of the Liver, Gallbladder and Bile Ducts, London, The Macmillan Company, 1929, p. 691.

8. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1928, p. 736.

9. Schröder, quoted by Naunyn: On Cholelithiasis, translated by the New Sydenham Society, London, 1896, p. 38.

10. Kaufmann, Edward: Pathology, Philadelphia, P. Blakiston's Son & Company, 1929, vol. 2, p. 1002.

11. Harley, G.: Diseases of the Liver, London, J. & A. Churchill, 1883, p. 575.

12. Kraus, J.: On Gallstones, English translation, London, Kegan & Paul, 1896, p. 2.

13. Colwell, H.: The Relation of Carcinoma to Gallstones, Arch. Middlesex Hosp., London **5**:123, 1905.

14. Moxon: Tr. London Path. Soc. **18**:140, 1868.

15. Proescher, F.: A Remarkable Case of Carcinoma of the Gallbladder in a Man Twenty-Two Years Old, J. A. M. A. **48**:481 (Feb. 9) 1907.

16. Haas, H.: Prag. Vitljhrschr. **132**:136, 1876.

17. Chavannaz: Gaz. hebd. de méd., Paris **6**:721, 1901.

18. Thomas, A., and Noica: Bull. Soc. anat. de Paris **71**:471, 1896.

19. Haberfeld: Ztschr. f. Krebsforsch. **7**:190, 1908.

20. Riedel: Berl. klin. Wchnschr. **38**:1, 1901.

The incidence is: (1) stomach, (2) colon (and cecum), (3) rectum, (4) esophagus and (5) gallbladder and ducts. Kaufmann [10] estimated carcinoma of the gallbladder as making up 5 per cent of all carcinoma found at autopsy. Smithies [21] found among 1,000 consecutive cases of gallbladder disease 23 cases of primary and 8 of secondary malignant disease. McCarty,[22] in a survey of 4,998 gallbladders removed at operation, found only 24 cases of carcinoma. Sherrill [23] and others reported that carcinoma is the most common tumor of the gallbladder.

PATHOLOGY

Histology.—Ewing [8] classified primary carcinoma of the gallbladder into the following groups according to the gross anatomy: (1) villous, papillomatous or fungating, (2) gelatinous and (3) diffuse, flat or infiltrating carcinoma.

As to the structural anatomy, he classified the types as follows: (1) adenocarcinoma, (2) alveolar carcinoma and (3) squamous cell carcinoma, either pure or associated with cylindric cell carcinoma.

Rolleston and McNee [7] classified carcinoma of the gallbladder histologically as columnar or spheroidal cell carcinoma, and stated that the cells may undergo colloid degeneration. The columnar cell carcinoma may grow into the cavity of the gallbladder as a villous tumor or a papilloma. Delafield and Prudden [24] and Treutlein [25] described the structure in the same manner. Rolleston and McNee [7] stated that in invasion of the deeper layers it does not show a papillary arrangement, but that ordinarily it is a columnar cell carcinoma with a fair amount of fibrous tissue. The cells of part of the growth may be columnar, of part cubical and of part spheroidal.

The large epithelial cells may even appear flattened. Multinuclear cells are seen at times. They added that as a result of metaplasia a squamous cell carcinoma of the gallbladder may occur and they collected 36 cases from the literature up to 1929. Similar cases have been described by Herxheimer,[26] Lubarsch,[27] Nicholson [28] and Simmonds.[29] Infiltration of the wall may occur without any villous projection into

21. Smithies, F.: Am. J. M. Sc. **157**:67, 1919.

22. McCarty, W. C.: Ann. Surg. **69**:131, 1919.

23. Sherrill, J. G.: Ann. Surg. **44**:866, 1906.

24. Delafield, F., and Prudden, T. M.: Pathology, New York, William Wood & Company, 1927, p. 861.

25. Treutlein, A.: Centralbl. f. allg. Path. u. path. Anat. **12**:825, 1901.

26. Herxheimer: Beitr. z. path. Anat. u. z. allg. Path. **41**:348, 1907.

27. Lubarsch, O.: Verhandl. d. deutsch. path. Gesellsch. **10**:198, 1906; Die Metaplasiefrage und ihre Bedeutung für die Geschwulstlehre, Arb. a. d. path. anat. Abt. d. k. hyg. Inst. zu Posen, 1901, p. 205.

28. Nicholson, G. W.: Path. & Bact. **13**:41, 1909.

28. Nicholson, G. W.: J. Path. & Bact. **13**:41, 1909.

the lumen of the gallbladder. Because of this the tumors are grouped as follows: (1) villous or papillomatous, (2) infiltrating and (3) gelatinous.

The latter is an infrequent form, usually filling the lumen of the gallbladder, and in women it may involve the ovaries by extension giving rise to one type of the so-called Krukenberg bilateral ovarian carcinoma.[30]

Site of Origin.—Rolleston and McNee [7] stated that one would conclude that carcinoma of the gallbladder arises from three locations, according to the descriptions of the earlier cases:

1. The fundus. It is the most dependent portion of the gallbladder and therefore particularly exposed to irritation from calculi.

2. The midportion. This produces the so-called hour-glass gallbladder.

3. The neck. Stones are often found impacted here.

However, the greater number are found involving the gallbladder so extensively that the site of origin cannot be definitely determined.

The Gallbladder.—Kaufmann [10] stated that the gallbladder is usually found distended, hydropic or filled with pus. It contains calculi in a large percentage of cases. Rarely the entire wall is infiltrated, forming a tumor the size of a fist or larger, containing stones and with very little of the gallbladder wall remaining. The carcinomatous gallbladder may shrink to a mass the size of a bean with its cavity containing calculi.

Extension.—Extension may occur by two methods: direct growth into the liver or by adhesions to any adjacent structure. It may grow into and along adjacent blood vessels.

By metastasis it may spread to the liver, giving scattered nodules. Rolleston and McNee [7] mentioned a case with white nodules of carcinoma in the serosa of the small intestine. Kaufmann [10] stated that metastases to the pouch of Douglas may predominate the picture, that metastasis to the regional lymph nodes is rare and that he has seen metatasis to the lung. Osler [31] reported a case with metatasis to the right breast. However, distant metastases are only rarely mentioned. Involvement of the liver was noted in 10 of our 19 cases, of the lymph nodes along the common duct in 8, of the peritoneum in

30. Krukenberg, F. E.: Arch. f. Gynäk. **50**:287, 1895-1896. Metzer, M. Leo: Metastases ovariques des cancers digestifs, Thèse, Paris, 1911, no. 354. Hall, M. E.: Proc. New York Path. Soc. **12**:57, 1912. Stone, W. S.: Surg., Gynec. & Obst. **22**:407, 1916. Major, R. H.: ibid. **27**:195, 1918. Delafield and Prudden (footnote 24).

31. Osler, W.: Brit. M. J. **1**:2, 1906.

2, of the colon in 1, of the bladder in 1 and of the lymph nodes along the aorta in 1.

Fistulas.—Perforation may occur into the colon, stomach or duodenum. Perforation into the colon occurred in 10 of the 100 cases collected by Musser.[6] Of Riedel's[32] 100 cases, 6 showed the same condition, perforation occurring into the stomach in 5 and into the duodenum in 10. One of our cases showed an old perforation into the colon.

Rolleston and McNee[7] called attention to the fact that this not infrequently occurs in cholelithiasis, so that in at least a part of these cases the perforation may well have occurred before the carcinoma developed.

Pressure Effects.—These effects may be classed into two groups. Pressure against the duodenum may be such that the findings simulate carcinoma or other stricture of the pylorus. Rabé and Rey[33] and Lejonne and Melanoff[34] reported this condition. One of our patients had definite duodenal obstruction due to pressure. In another, the colon was obstructed but only partly.

Closure of the portal vein and its associated group of findings may be caused either by pressure or by direct invasion of the vein. This was found as the etiologic factor in 6 of 68 cases of pylephlebitis collected by Lissauer.[35] In 2 of our cases there was definite obstruction of the hepatic duct due to the pressure of metastases. In another there was apparently intermittent obstruction of the cystic duct causing recurrent enlargement of the gallbladder, but this may have been caused by the contained stones.

ETIOLOGY

Relation of Carcinoma (At Any Site in the Body) to Gallstones.—This subject is slightly aside from the one under discussion but is of interest indirectly and is mentioned in order to discuss what appears to us to be an apparently mistaken assumption.

Colwell,[13] in 1905, reported the following: Among 11,400 autopsies from 1854 to 1899 at the Middlesex Hospital, gallstones occurred in 359, or 3 per cent. Among 1,886 autopsies from 1900 to 1904, gallstones were found in 102, or 5.7 per cent. Colwell's figures from 1854 to 1904 for the relative occurrence of gallstones in cases of carcinoma (at any site in the body) in the two sexes were approximately proportional to the liability of males and females to cancer. In the autopsies from 1900 to 1904, gallstones were found in both sexes

32. Riedel: München. med. Wchnschr. **58**:1337, 1911.
33. Rabé and Rey: Bull. Soc. anat. de Paris **72**:881, 1897.
34. Lejonne and Melanoff: Bull. Soc. anat. de Paris **75**:133, 1900.
35. Lissauer: Virchows Arch. f. path. Anat. **192**:278, 1908.

approximately two and one-half times as frequently in carcinomatous as in noncarcinomatous cases. At first glance this would suggest that the occurrence of cancer at any site in the body predisposes that person for some reason to the formation of gallstones. However, as the age incidence of gallstones and cancer falls within much the same limits, this seeming direct relation probably is only incidental.

General.—In summing up the factors concerned in the etiology of carcinoma of the gallbladder, Ewing [8] stated that the following combine in producing the remarkable susceptibility of the mucous membrane of the gallbladder to the formation of carcinoma: (1) mechanical irritation of calculi, (2) catarrhal inflammation that excites a cellular overgrowth, (3) the relation to a peculiar form of lipoid metabolism (cholesterol) and (4) irritative and digestive action of the bile.

Relation to Gallstones.—The occurrence of gallstones in carcinomatous gallbladders is unquestionably greater than that in noncarcinomatous gallbladders. Of course, the question arises as to whether or not the stones form after the carcinoma, but in a great many cases the history of cholecystitis and cholelithiasis precedes the most remote time at which the carcinoma might have originated. Those authors favoring the theory that carcinoma is the cause of the increased incidence of stones state that the growth favors infection, stagnation and cholecystitis, and consequently the formation of stones.

However, if this were entirely correct, the incidence of stones should be approximately the same in primary and secondary carcinoma of the gallbladder. As against this, Siegert [36] collected 99 cases of primary carcinoma of the gallbladder with stones in 94. In his 13 cases of secondary carcinoma of the gallbladder stones were found in only 2. Rolleston and McNee [7] reported 25 additional cases of secondary carcinoma of the gallbladder with stones found in only 1. This gives an occurrence of stones in cases of secondary carcinoma of the gallbladder of 8 per cent, which is within the limits of the expectance of gallstones. (Schröder [9] estimated that from 5 to 12 per cent of all autopsies done as a routine measure show gallstones.) Of course, secondary carcinoma ordinarily occurs under the mucosa while primary carcinoma is in the lumen of the gallbladder and would therefore be a more important factor in the production of stones.

In Schröder's [9] 120 cases of gallstones there were 20 cases of primary carcinoma of the gallbladder (14 per cent). Fawcett and Rippmann [37] reported 592 cases of gallstones from the postmortem records of Guy's Hospital with 48 cases of carcinoma of the gallbladder and cystic duct (12.3 per cent). Riedel [32] estimated that from 7 to 8 per

36. Siegert, F.: Virchows Arch. f. path. Anat. **132**:353, 1893.
37. Fawcett, J., and Rippmann, C. H.: Guy's Hosp. Rep. **67**:41, 1913.

cent of cases of cholelithiasis showed carcinoma. Rolleston and McNee [7] reported 300 cases of gallstones from St. George's Hospital with 13 cases of carcinoma (4.3 per cent), but they stated that among the 300 cases were included many showing only minute bilirubin calcium stones and gave this as the reason for the low incidence.

Slade [38] found carcinoma in 10 cases among 17 gallbladders (59 per cent) with chronic inflammatory changes associated with gallstones; all but 1 of the patients had died from the effects of the gallstones. In 5 of these the carcinoma could be demonstrated microscopically only.

In patients with mental disease (i. e., in patients brought into the hospital always for some reason other than symptoms referable to the gallbladder or to cancer), Candler [39] found only 2 cases of primary carcinoma of the gallbladder in 315 cases of gallstones (less than 1 per cent). The implication in this is that those patients with gallstones and cancer, being more seriously ill, are taken to hospitals, and the incidence in the hospitals is thus increased far beyond the actual incidence in the general population.

Approaching the question from the other side, we have the following figures on the incidence of gallstones in cases of carcinoma of the gallbladder. In 14 of our 19 cases stones were noted (73.7 per cent). They ranged in number from a solitary stone to more than 60. In some of the cases only a cholecystostomy or biopsy was done, and at least a part of these may have had unnoticed stones.

The incidence in various groups of collected cases is a follows:

Incidence of Stones

	Number of Cases	Percentage With Stones
Musser [6]	100	69
Fütterer: Ueber die Aetiologie des Carcinomas, Wiesbaden, J. F. Bergmann, 1901, p. 55; Festschr. f. G. E. von Rindfleisch, Leipzig, 1907, p. 89	268	70
Haberfeld [19]	190	70
Zenker: Deutsches Arch. f. klin. Med. **44**: 159, 1888-1889	159	85
Courvoisier: Pathologie und Chirurgie der Gallenwege, Leipzig, F. C. W. Vogel, 1890, p. 375	103	91
Siegert [36]	...	95
Janowski: Beitr. z. path. anat. u. z. allg. Path. **10**: 449, 1891	...	100

There is undoubtedly some duplication of cases in part of these compilations. The incidence, however, is great enough to suggest a definite relationship between the irritation of the calculi, the associated cholecystitis and the carcinoma formation.

Erdmann [40] reported that in a series of 224 consecutive operations for cholecystitis 15 cases showed carcinoma of the gallbladder. In 1,000

38. Slade: Lancet **1**:1059, 1905.

39. Candler: Proc. Roy. Soc. Med. **4**:87, 1911.

40. Erdmann, J. F.: Am. J. Obst. **80**:618, 1919.

operations for gallstones, Deaver [41] found malignancy in 16. Smithies [21] reported 23 in 1,000 operations on the gallbladder. Schnabel [42] reported a case in which carcinoma of the gallbladder developed long after an incomplete cholecystectomy. Coates [43] reported a case in which carcinoma of the gallbladder developed seven years after a calculus was removed.

Lazarus-Barolow [44] put forth a unique idea. He reported that calculi removed from patients with carcinoma of the gallbladder contained more radioactive materials than other gallstones. In the literature we could find no confirmation of this finding.

Leitch,[45] in 1924, produced carcinoma in the gallbladder of guinea-pigs experimentally by inserting human gallstones, pebbles and pitch into the gallbladder. In a small series of cases the incidence of carcinoma formation was greater with the pebbles or pitch. He stated that this was the first time glandular carcinoma had been developed experimentally. Debbet and Godard,[46] in 1928, reported having produced carcinoma by inserting gallstones from cancerous human gallbladders into the gallbladders of guinea-pigs.

One of us (Dr. Shelley) recently reported a case in which a good-sized piece of tape had remained in a patient's gallbladder for a period of eighteen years. Careful microscopic examination of this gallbladder revealed no carcinoma cells.

CLINICAL PICTURE

Rolleston and McNee [7] stated that the symptoms of carcinoma of the gallbladder may be referred to: (1) a preexisting cholelithiasis and cholecystitis, (2) the local effects of the carcinoma in the gallbladder and (3) the more distant effects due to extensions and metastases—to which should be added the general or constitutional effects of malignancy.

Ewing [8] stated that the initial symptoms may be local pain or dyspepsia, but that a local tumor is the first symptom in 50 per cent of the cases. He stated also that jaundice suddenly established and persistent occurs in most cases, although some authors do not give this symptom such prominence. Ascites is often added from throm-

41. Deaver, J. B., and Ashhurst, S. P. C.: Med. Rec. **96**:47, 1919; Surgery of the Upper Abdomen, ed. 1, Philadelphia, P. Blakiston's Son & Company, 1909, p. 218; Am. J. Surg. **38**:105, 1924.

42. Schnabel, T. G.: Am. J. M. Sc. **162**:95, 1921.

43. Coates, H. W.: Clinical Hour **58**:54 (Jan. 30) 1929.

44. Lazarus-Barolow, W. S.: Brit. M. J. **1**:95, 1914.

45. Leitch, A.: Brit. M. J. **2**:451, 1924.

46. Debbet, Paul; and Godard, H.: Bull. Assoc. franç. p. l'étude du cancer **17**:347 (June) 1928.

bosis of large veins or peritoneal metastases, and the effusion may be chylous. He added that the cachectic stages are marked by fever from infections, cholemia, hemorrhages and emaciation. The total duration is extremely variable, some cases never being suspected until autopsy. After the appearance of jaundice few patients live more than six months.

There may or may not be a history of attacks of gallstone colic and cholecystitis. Kehr [47] found the symptoms of gallstones absent in the majority of his cases. Jourdan [48] reported a case in which there was a history of colics for twenty-five years before the carcinoma was found. Bret [49] reported the case of a woman who died at the age of 36 of carcinoma of the gallbladder which contained an oval calculus. She had had gallstone colics for the sixteen preceding years. Many patients found to have carcinoma of the gallbladder have had no symptoms of gallstones, but, of course, many patients are found to have gallstones who have never had symptoms. Magoun and Renshaw [50] reported that in their 84 cases they found that the duration of symptoms ranged from one month to forty years. The average loss of weight was 15 pounds (6.8 Kg.), the greatest 50 pounds (22.7 Kg.). Sixty patients gave a definite history of gallstone colic. Thirty-two complained of a dull pain with or without colic. Forty patients had varying degrees of jaundice. Twenty-three gave a history of fever.

Rolleston and McNee [7] described the course of a typical case having symptoms as follows: If there is a history of colics or cholecystitis, there is no change in the clinical picture at the onset of the growth. Later, continuous pains, a hard, rough gallbladder continuously increasing in size, and the general symptoms of a malignant condition may appear.

Cases are not uncommon in which no symptoms had pointed to the gallbladder as the source of a patient's metastatic carcinoma. Osler [51] reported a case of carcinoma of the right breast found later to be a metastasis from a primary carcinoma of the gallbladder. Two cases are reported by Rolleston and McNee [7] from St. George's Hospital, one a case with ascites and no jaundice diagnosed as cirrhosis of the liver. At autopsy, a primary carcinoma of the gallbladder was found containing stones. Metastases to glands behind the pancreas had compressed the portal vein, causing ascites. The second case showed a metastatic growth in the spine simulating caries. Later, a carcinoma of the gallbladder was found to be the source.

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47. Kehr: Diagnosis of Gallstone Disease, Philadelphia, 1901, p. 92.
48. Jourdan: Bull. soc. anat. de Paris **66**:323, 1891.
49. Bret: Lyon méd. **89**:35, 1898.
50. Magoun, J. A. H., Jr., and Renshaw, K.: Ann. Surg. **74**:700, 1921.

Symptoms referable to gallstones in our 19 cases are: Only 5 patients gave a history of typical gallstone colics; 2 gave a history of milder but more continuous pain in the right upper quadrant of the abdomen referred to the right shoulder and 2 had had chills and fever. Local symptoms referable to the tumor are: jaundice in 8 cases, pain in the right upper quadrant in 8 and palpable tumor in 9. The only general symptom of carcinoma was loss of weight as noted in 8 cases, the greatest amount being 25 pounds (11.3 Kg.), and one case with marked loss of strength.

Symptoms of Liver Invasion.—The symptoms due to invasion of the liver are the same as those of any other cancerous invasion of the liver. It may be enlarged. The surface is smooth or nodular, according to the type of involvement. The bile ducts may become involved with jaundice resulting. The various groups of collected cases show jaundice in from 60 per cent up, although in a part of these it was found to be due to some associated condition, such as stones in the hepatic or common ducts and cholangeitis. Jaundice was present in 8 of our cases, in 2 of which there were common duct stones.

Distant Effects.—The more distant effects are those of any malignancy—anemia, cachexia and the like. It is very interesting to note that among the 9 cases in our list in which hemoglobin determinations and red counts were made, 7 showed normal findings, 1 slight anemia, and only 1 a severe anemia. Judd and Baumgartener [51] also noted that anemia is almost never associated with malignancy of the gallbladder.

Ascites due to peritoneal implants or obstruction of the portal vein is not uncommon. Secondary growths may cause obstruction of the pylorus or colon. Breaking down of the carcinoma tissue may cause perforation or abscess formation. Ascites was noted as present in 2 and loss of weight and cachexia in 8 of our cases.

DIAGNOSIS

In a large percentage of cases the diagnosis of carcinoma of the gallbladder cannot be made without direct examination by operation. A great many are never suspected and are found only at autopsy. Ordinarily, when a positive diagnosis can be made preoperatively, it is too late to operate.

The condition should be suspected in a patient with a history of gallstone colics or attacks of cholecystitis who has a continuous and increasingly severe pain in the epigastrium or the right side of the

51. Judd, F. S., and Baumgartner, C. J.: Malignant Lesions of the Gallbladder, Arch. Int. Med. **44**:735 (Nov.) 1929.

hypochondrium, loss of appetite and a nodular tumor increasing in size in the location of the gallbladder.

Roentgen Examination.—A positive diagnosis can be made if the outline of the tumor shows with the dye in a roentgenogram. Failure of the gallbladder to fill is suggestive and is the most common finding. Graham and Cole,[52] Whitaker, Milliken and Vogt[53] and Carman[54] concur in this. Cholecystograms were made in but 2 of our cases, and in both the gallbladder did not fill.

Kirklin[55] reported 20 cases with a diagnosis of papilloma of the gallbladder, in 4 of which operation was performed and the diagnosis confirmed. He found that papillomas have definite roentgenologic characteristics: The shadows retained the same position in all films in which they appeared. The small round defects were never more than 1 cm. in diameter, and never immediately at the fundal pole, but often were marginal. The defects might be single or might be three or more, but they were always discrete. Frequently the defects were clear and usually most clearly visible at the twentieth hour after oral administration of the dye. He hoped that this finding might aid in the diagnosis of carcinoma of the gallbladder in its earlier stages.

DIFFERENTIAL DIAGNOSIS

Gallstones and Cholecystitis.—The symptoms of carcinoma of the gallbladder and gallstones and cholecystitis are much the same, and often the symptoms of cancer are merely grafted onto those of a preexisting diseased condition of the gallbladder. A very thick, chronically inflamed gallbladder wall may look like carcinoma even when opened and examined. Dense adhesions in the right upper quadrant are found in both conditions. Stones in the common duct may feel like glands invaded by carcinoma. Microscopic examination at times reveals carcinoma in a gallbladder wall removed for some other condition and not previously suspected.

Malignant Disease of the Liver.—Primary malignant disease of the liver or carcinomatous metastasis, whether from the gallbladder or

52. Graham, E. A., and Cole, W. H.: Roentgenologic Examination of Gallbladder, New Method Utilizing Intravenous Injection of Tetrabromphenolphthalein, J. A. M. A. **82**:613 (Feb. 23) 1924. Graham, E. A.; Cole, W. H., and Copher, G. H.: Visualizing of Gallbladder by the Sodium Salt of Tetrabromphenolphthalein, ibid. **82**:1777 (May 31) 1924.

53. Whitaker, L. R.; Milliken, G., and Vogt, E. C.: Surg., Gynec. & Obst. **40**:847, 1925.

54. Carman, R. D.: Lancet **2**:67, 1925.

55. Kirklin, B. R.: Proc. Staff. Meet., Mayo Clin. **5**:336 (Nov. 19) 1930; Cholecystographic Diagnosis of Papillomas of the Gallbladder, Am. J. Roentgenol. **25**:46 (Jan.) 1931.

other sources, presents the same picture. A preceding history referable to the gallbladder suggests that organ as the origin of the growth.

Carcinoma of the Stomach.—Carcinoma of the gallbladder may cause pyloric obstruction by pressure. A barium sulphate meal and roentgenograms may differentiate the causes of the obstruction. There should be a difference in the early history of the two conditions.

Carcinoma of the Hepatic Flexure of the Colon.—Invasion of the colon by the carcinoma of the gallbladder may give the same symptoms as carcinoma of the colon. The previous history together with roentgen examinations of the stomach, gallbladder and colon may differentiate the two.

Carcinoma of the Head of the Pancreas and Bile Ducts.—Late in the disease the similarity between this condition and carcinoma of the gallbladder is so close that it is often impossible to differentiate them. Also both may have been preceded by a history typical of gallstones or cholecystitis.

Syphilis.—Syphilitic disease of the liver, particularly with a gumma in the region of the gallbladder, may give much the same picture as carcinoma of the gallbladder. A positive Wassermann reaction, of course, does not rule out carcinoma, nor a negative one syphilis.

Other Conditions.—Gerhardt [56] reported a case in which from scar contraction and deformity a piece of the right lobe became elongated and hard so that during life it was thought to be a carcinoma of the gallbladder.

TREATMENT

Prophylactic.—Removal of gallbladders from patients who have a history of gallstone colics or attacks of cholecystitis and of those in whom stones are found accidentally may prove to be of value in the prevention of the development of carcinoma of the gallbladder. Judd and Baumgartner [51] stated that at the Mayo Clinic the frequency of the occurrence of malignant disease of the gallbladder had diminished from 5 per cent in the earlier years to 0.5 per cent in later years. They attributed this to the fact that diseased gallbladders are now removed much earlier.

Medical.—Medical treatment is only palliative and is used in relieving the symptoms as they arise. Roentgen treatment may relieve some of the symptoms temporarily.

Surgical.—Surgical removal presents the only hope of cure at the present time, but diagnosis is nearly always made so late that an attempt at complete removal cannot be made. Except in the rare cases in which the growth is very small and limited to the free portion of the gallbladder wall, the operative mortality is very high. In many cases

56. Gerhardt: Semaine méd. **18**:273, 1898.

attempted removal is contraindicated, but various surgical procedures to relieve conditions caused by the growth may be indicated.

PROGNOSIS

The various reports of percentages of surgical cures varies from none to 6 per cent. Fourteen of our patients died in the first three weeks after operation. Of the remaining 5, 1 died in one month, 3 died at six months of metastases and 1 is living and well at six and one-half years.

Quinn [57] collected 57 cases in which carcinomatous gallbladders had been removed. Fifty of the patients died within a year. This includes the immediate operative mortality. Two died at the end of a year. Five were reported living, 1 at eight months, 1 at two years and two months, 2 at three years and 1 at four years and six months. Magoun and Renshaw [50] reported a series of 84 cases in which operation disclosed malignancy of the gallbladder. The operative mortality was 8, just under 10 per cent. Of the 29 patients on whom only explorations were done and who were later traced, the greatest length of life was three years. Of the 26 on whom cholecystectomy was done and who were later traced, 6 were still alive, 3 at two years, 1 at eight years, 1 at nine years and 1 at eleven years. The last showed the greatest length of life for the group. Twelve did not live longer than a year. The remaining deaths were fairly evenly divided among the years to eleven.

Webber,[58] in reporting 30 cases of primary carcinoma of the gallbladder in 1927, classified them into four grades according to the differentiation of the carcinoma cells. Two patients, both with grade II carcinoma, were still living at the time the report was made, 1 at thirteen months and the other at seventy-nine months. The average lengths of life of patients with grade I carcinoma was sixteen months; with grade II, ninety-two and three-tenths months; with grade III, seven and five-tenths months; with grade IV, thirteen months. Webber concluded that determination of the grade of malignancy through a study of the cell differentiation in a microscopic section of the tumor appeared to be a definite aid in estimating both the likelihood of metastasis and the relative length of life of the patient after operation.

Even in those cases in which the growth at the time of removal was very small, early and extensive recurrence and metastases are frequently the outcome. Heidenhain [59] removed a gallbladder containing six stones. A button-like thickening on the gallbladder wall proved to be carcinoma, microscopically. The patient died of metastases in the liver three months

57. Quinn, M.: Bull. et mém. Soc. d. chirurgiens de Paris **34**:215, 1908.

58. Webber, I. M.: Surg., Gynec. & Obst. **44**:756 (June) 1927.

59. Heidenhain: Verhandl. d. deutsch. Gesellsch. f. Chir., 1898, p. 126.

later. At the time of operation the liver had been found smooth. One of our cases was similar to this in every detail.

REPORT OF CASES

CASE 1.—Mrs. E. R., white, aged 64, a housewife, entered the hospital on Jan. 10, 1916, because of acute severe pain in the right upper quadrant. The white cell count was 29,000, with polymorphonuclear leukocytes 82, and lymphocytes 18.

Operation revealed a gangrenous gallbladder connected with the transverse colon by a fistulous opening. There were many stones in the gallbladder, and one was removed from the common duct. The gallbladder was removed.

Microscopic examination showed carcinoma of the gallbladder which was acutely infected and contained areas of gangrene.

The patient died a few hours after operation.

CASE 2.—Mr. J. F., white, aged 65, no occupation, entered the hospital on Jan. 12, 1916, because of pain in the right upper quadrant. Operation revealed a thickened gallbladder containing stones. A diagnosis of carcinoma was made and cholecystectomy done. There were many adhesions about the cystic duct, probably due at least in part to extension of the carcinoma. Microscopic examination confirmed the diagnosis of carcinoma.

The patient was discharged on the sixteenth day after operation with the wound healed, but died six months later of metastases.

CASE 3.—Mr. N. M. L., white, aged 53, a physician, entered the hospital on Jan. 12, 1916, because of pain in the right upper quadrant. Operation revealed the gallbladder a solid mass of carcinoma and the entire liver riddled with metastases. A piece was removed for examination, and the abdomen closed. Microscopic examination showed the tumor to be an adenocarcinoma.

The patient left the hospital on the nineteenth day after operation with his wound healed, but died six months later of metastases.

CASE 4.—Miss F. C., white, aged 53, a dressmaker, entered the hospital on June 5, 1916, because of generalized abdominal pain of four months' duration. For four weeks she had been jaundiced and losing weight. Examination revealed a large mass in the right upper quadrant which moved with respiration and was not tender. A plain plate of the abdomen showed no abnormal shadows. Operation revealed a carcinoma of the gallbladder with metastasis in the liver. Cholecystectomy was done. The section of a piece of the tumor from the gallbladder showed carcinoma with an acute inflammatory reaction.

The patient died on the sixth day after operation.

CASE 5.—Mrs. H. G. W., aged 54, a housewife, entered the hospital on May 29, 1917, because of attacks of pain in the right upper quadrant. At operation, a thickened carcinomatous gallbladder was found adherent to the liver, and containing stones. The lymph nodes along the common duct were involved. The stones were removed and a cholecystostomy done. Microscopic examination of one of the lymph nodes showed carcinoma.

The patient was discharged with the wound healed on the eighteenth day after operation, but died eight months later of generalized metastases.

CASE 6.—Miss G. F., white, aged 53, a nurse, entered the hospital on Nov. 1, 1917, because of an acute attack of pain in the right upper quadrant. The blood count was: hemoglobin, 55 per cent; red blood cells, 3,000,000; white blood cells, 10,000; polymorphonuclear leukocytes, 70, and lymphocytes, 30. At operation, the gallbladder had the appearance of acute cholecystitis. It was removed, and the

common duct explored. No stones were found. The microscopic report was carcinoma of the gallbladder.

The patient died four months after operation of peritoneal and pulmonary metastases.

CASE 7.—Miss N. F., white, aged 52, no occupation, entered the hospital on Jan. 22, 1918. For six months she had had intermittent pain in the right upper quadrant, radiating to the back and associated with gaseous eructations. During this time she had lost 20 pounds (9 Kg.) in weight. For two weeks she had been jaundiced. No tumor could be felt. Operation revealed a thickened gallbladder containing stones. The cystic duct was completely closed, and the mass compressed the hepatic duct. The liver was involved by direct extension. Cholecystectomy was done. Microscopic examination showed carcinoma of the gallbladder with acute inflammation.

Death occurred on the ninth day after operation.

CASE 8.—Mrs. J. R., white, aged 53, a housewife, entered the hospital on April 13, 1918, because of pain in the right upper quadrant, radiating to the back and right shoulder, which had been present for seven weeks. For ten days she had been jaundiced, but the color of the stools had not been noted. The blood count was: hemoglobin, 75 per cent; red blood cells, 5,000,000; white blood cells, 9,000; polymorphonuclear leukocytes, 78, and lymphocytes, 22. The liver was large and nodular, extending 3 inches (7.6 cm.) below the costal margin. At operation, the gallbladder was found to be a mass of carcinoma firmly attached to the liver, which was also extensively involved, as were the lymph nodes along the common and hepatic ducts. Microscopic examination of a lymph node showed alveolar carcinoma.

The patient left the hospital on the eighteenth day, the wound having healed by primary union, but she failed to return for follow-up examination.

CASE 9.—Miss M. C., white, aged 53, no occupation, entered the hospital on July 26, 1919, because of pain in the right upper quadrant with jaundice of several weeks' duration. A general debility had been noticed for several months. The blood count was: hemoglobin, 88 per cent; red blood cells, 4,600,000; leukocytes, 6,600; polymorphonuclear leukocytes, 55, and lymphocytes, 35. The coagulation time was four and one-half minutes. Operation revealed a gallbladder with the gross appearance of carcinoma which was adherent to all adjacent structures. It contained stones, and one was also removed which blocked the common duct. No metastases could be found in the liver or adjacent glands. Cholecystectomy was done. The microscopic diagnosis was medullary carcinoma of the gallbladder with invasion of the attached pieces of liver tissue.

Death occurred on the eighth day after operation.

CASE 10.—Mrs. M. G., white, aged 62, a housewife, entered the hospital on July 13, 1922, because of vomiting. This had been present for three weeks and occurred one hour after each meal. She had lost 18 pounds (8.2 Kg.) in the month before admission. A mass could be felt in the right upper quadrant. Two and one-half quarts of fluid was obtained by gastric lavage. The free hydrochloric acid was 6 and the total acid 30. Roentgenograms of the gastro-intestinal tract showed a deformed duodenal cap and retention in the stomach at twenty-four hours. The blood count was: hemoglobin, 88 per cent; red blood cells, 3,700,000; white blood cells, 8,400; polymorphonuclears leukocytes, 71; lymphocytes, 28, and basophils, 1 per cent. At operation a greatly thickened gallbladder was found with all the adjacent glands involved. Cholecystectomy and excision of one gland was done. The gallbladder contained one stone. Microscopically, the gallbladder and gland showed a mucoid type of carcinoma.

The patient died immediately after operation, and an autopsy showed extensive metastasis to the liver and the glands along the aorta. The ovaries were normal.

Case 11.—Mrs. M. B., white, aged 54, a housewife, entered the hospital on Sept. 12, 1922, because of epigastric pain which radiated to the right scapula and which had been present for eight days. Jaundice had been noticed with dark urine and clay-colored stools for six days. For some time previously the patient had been losing weight. The blood urea was 12.5 mg., and the blood sugar 105 mg. per hundred cubic centimeters of blood. An orange-sized mass could be felt at the margin of the liver.

Fig. 1.—Specimen from case 11. The gallbladder is laid open. The carcinoma can be seen at the fundus, involving more than half of the gallbladder. The loose stones came chiefly from the uninvolved portion; the others lie as found.

Operation revealed a large thick gallbladder containing more than sixty stones (fig. 1). The hepatic duct was obstructed by the pressure of metastases in the lymph nodes. Cholecystectomy with drainage of the hepatic and common ducts was done. The microscopic diagnosis was adenocarcinoma of the gallbladder.

The patient was discharged twenty-six days after operation with no drainage and only slight jaundice. When last seen one year after operation, she was fairly well and only slightly jaundiced.

Case 12.—Mrs. F. M., white, aged 49, a housewife, entered the hospital on Aug. 25, 1923. Five weeks before she had had a sharp severe pain in the right

upper quadrant which radiated to the back and right shoulder. Two days later she became jaundiced. These symptoms persisted to the time of admission. Ten and three months before admission she had had similar attacks. For ten months she had had gaseous eructations, and during this time had lost 25 pounds (11.3 Kg.) in weight.

A plain plate of the abdomen showed nothing abnormal. Roentgenograms of the gastro-intestinal tract showed a spasm of the pylorus which was reported as probably due to gallbladder disease. A test meal gave free hydrochloric acid 54 and total acid 90. The blood count was: hemoglobin, 100 per cent; red blood cells, 5,100,000; white blood cells, 7,400; polymorphonuclear leukocytes, 64, and lymphocytes, 36. The coagulation time was four and one-half minutes.

Operation revealed a carcinomatous gallbladder containing six stones. It appeared to be acutely inflamed. The nodes along the biliary ducts were involved. Cholecystectomy with choledochostomy was done. The diagnosis was confirmed by microscopic examination.

The patient died four hours after operation.

CASE 13.—Mrs. A. D., white, aged 68, a housewife, entered the hospital on June 13, 1924, because of a lump which had been noticed in the right upper quadrant for the preceding five months. With this she had had recurrent attacks of vomiting, pain in the right upper quadrant and constipation. She had lost weight for six months. A mass could be felt in the right upper quadrant. A preoperative specimen of urine showed 1.7 per cent sugar with acetone and diacetic acid. The postoperative specimen contained the same.

At the operation the gallbladder was definitely carcinomatous, but no metastases were noted. It contained twenty-five stones (fig. 2). Cholecystectomy was done. The diagnosis of carcinoma was confirmed by microscopic examination.

The patient died one day after operation in diabetic coma.

CASE 14.—Mr. H. S., white, aged 62, a barber, entered the hospital on March 1, 1925, because of intermittent attacks of pain in the right upper quadrant which radiated to the back. From the age of 17 to 35 he had had attacks of the same pain associated with chills, fever, vomiting and jaundice. A small rounded mass could be felt in the right upper quadrant. The laboratory findings were: hemoglobin, 92 per cent; red blood cells, 4,600,000; urea, 14.3 mg. per hundred cubic centimeters of blood, and phenolsulphonphthalein output, 52 per cent.

The operative findings were those of cholecystitis and cholelithiasis. Cholecystectomy was done. Examination in the laboratory revealed a small carcinoma in the fundus. This was verified by microscopic examination.

The patient made an uneventful recovery, and at the present time is alive and free from symptoms, more than six years later.

CASE 15.—Miss S. S., white, aged 48, a painter, entered the hospital on Feb. 27, 1925, complaining of epigastric pain in the right upper quadrant which radiated to the back and right shoulder. This had been present for three months. Jaundice, clay-colored stools and nausea, but no vomiting, had been present for six weeks. The bile index was 143, and the urine contained much bile. Exploratory laparotomy revealed a shrunken distorted gallbladder and carcinomatous nodules in the liver. Biopsy showed mucoid carcinoma. There was no ascites.

Following operation, the patient became apathetic, gradually failed, went into collapse and died six days after operation.

CASE 16.—Mrs. F. G., white, aged 55, a housewife, entered the hospital on Oct. 24, 1927, because of pain in the right upper quadrant radiating to the back and

right shoulder, associated with vomiting and gaseous eructations. She had been having such attacks for nineteen years. No masses could be felt. The blood count was: hemoglobin, 86 per cent; red blood cells, 4,600,000; white blood cells, 6,800; polymorphonuclear leukocytes, 64, and lymphocytes, 36. The blood urea was 10 mg. and the uric acid, 4.2 mg. per hundred cubic centimeters of blood. The phenolsulphonphthalein output was 50 per cent.

The operative diagnosis was cholecystitis and cholelithiasis. Cholecystectomy was done. When the gallbladder was opened, a papillary adenocarcinoma and one stone were found. This diagnosis was confirmed microscopically.

The patient was discharged with the wound completely healed on the seventeenth day after operation and died twenty-one months later of metastases in the liver.

Fig. 2.—Specimen from case 13. Tarry bile can be seen oozing from the cut cystic duct of the unopened specimen. The nodular appearing protuberance is the carcinoma at the fundus, a cross-section of which is seen in the opened specimen. The irregular objects outside of the gallbladder are partly necrotic portions of the papillary outgrowth from the cancer which broke off when the specimen was opened.

Case 17.—Mr. J. B., white, aged 61, a manufacturer, entered the hospital on May 28, 1929. For the preceding six weeks he had recurrent attacks of acute pain in the right upper quadrant radiating to the right shoulder. With this there were usually vomiting and jaundice. One year before he had a similar attack without jaundice. There was a palpable mass in the gallbladder region. The blood count was: hemoglobin, 93 per cent; red blood cells, 4,600,000; white blood cells, 11,800; polymorphonuclear leukocytes, 72, and lymphocytes, 28.

At operation, a hard indurated mass filled the gallbladder region. It was opened, and three stones were found and removed. The tissue about them appeared necrotic. Cholecystostomy was done. All adjacent structures were extensively involved by

direct extension of the carcinoma. The diagnosis was confirmed by microscopic examination.

The patient died three days after operation.

CASE 18.—Mrs. L. K., white, aged 65, a housewife, entered the hospital on Sept. 8, 1929, because of jaundice and loss of 15 pounds (6.8 Kg.) in weight in the four weeks preceding. She had had recurrent attacks of severe pain in the right upper quadrant for fifteen years. No mass was felt. The blood urea was 19.2 mg. per hundred cubic centimeters of blood. The bile index was 50. The coagulation time was five minutes and the bleeding time three minutes.

At operation, a thickened friable gallbladder was found which contained stones. It tore off while being removed. The common and hepatic ducts were explored but no stones found. Microscopic examination showed carcinoma of the gallbladder wall.

Death occurred nine days after operation.

CASE 19.—Mr. L. M., white, aged 70, no occupation, entered the hospital on Aug. 12, 1930. He had been coming in at intervals over a period of eighteen years for treatment for an old cerebrospinal syphilis. At various times he had complained of indigestion and pain in the right upper quadrant. Two roentgenographic series of the gastro-intestinal tract made four and five years before admission were reported normal.

On entrance to the hospital, the patient complained of a severe pain associated with nausea and vomiting of two weeks' duration. The bile index was 13. The blood count was: hemoglobin, 88 per cent; red blood cells, 4,000,000; white blood cells, 8,400; polymorphonuclear leukocytes, 88, and lymphocytes, 12. A mass could be palpated in the right upper quadrant which was very tender. This disappeared in about ten days, and the pain disappeared at the same time. With the recurrence of pain, the mass reappeared. The patient had a septic temperature, ranging from 101 to 105 F.

The first cholecystogram showed faint filling; a second showed none. Roentgenograms of the gastro-intestinal tract revealed a constant deformity of the first and second parts of the duodenum, attributed to adhesions. A clysma indicated adhesions about the hepatic flexure.

Operation revealed a large gallbladder adherent to all adjacent structures. It was white and filled with a gelatinous material in which were several stones. The liver, adjacent glands and peritoneum contained many metastases. The peritoneal cavity contained a small amount of serosanguineous fluid. A culture from the gallbladder grew Bacillus coli. Microscopic examination confirmed the diagnosis of carcinoma.

The patient died of generalized metastases six months after operation.

NOTE: These patients were operated on by the various members of the surgical staff of St. Luke's Hospital and the case reports are presented here with their permission. Case 19 is the only case in which operation was performed personally by the authors.

Only those cases in which the carcinoma was found at operation and the diagnosis confirmed by microscopic examination are included in this list which covers the period from 1916 to 1930, inclusive. Eleven other cases of carcinoma of the gallbladder were found at operation before 1916 at St. Luke's Hospital, but their records were too incomplete to be included in this present report. Their diagnoses were all confirmed by microscopic examination, however.

The comprehensive discussion of the subject by Rolleston and McNee in their book has been of the utmost value in the preparation of this paper.

1148 Fifth Avenue.

ENDOTHELIOMA OF THE DURA (MENINGIOMA)

REPORT OF AN UNUSUAL CASE

GEORGE G. DAVIS, M.D.
AND
H. C. VORIS, PH.D., M.D.
CHICAGO

The term endothelioma of the dura has been more or less successfully retained in the literature in spite of the fact that the true origin of these tumors is probably from the leptomeninges. Schmidt,[1] Weed[2] and Cushing and Weed[3] called attention to frequent calcareous deposits in the arachnoid membrane of man and adult lower mammals and their association with nests of cells due to hyperplasia of the arachnoid mesothelium. They emphasized that the so-called dural endotheliomas show histologically the same cellular arrangement as these nests of cells, and that hence they probably take their origin from the arachnoid mesothelium. Cushing preferred to refer to them as meningiomas. Mallory[4] discussed in detail the structure of these tumors and followed the authors named in ascribing their origin to the fibroblasts of the arachnoid villi. He suggested the term arachnoid fibroblastoma for these tumors, and considered them closely related to the tumors developed from the perineurium of the peripheral nerves, which he designated as perineurial fibroblastoma. Van Wagenen[5] and Penfield[6] followed Mallory in this usage. We have retained the term endothelioma of the dura on account of the physical relationship of these tumors to the dura and to conform to ordinary clinical usage in referring to these tumors.

From the Neurological and Surgical Service of the Cook County Hospital.

1. Schmidt, M.: Ueber die pacchionischen Granulationen und ihr Verhaeltnis zu den Sarkomen und Psammomen der Dura mater, Virchows Arch. f. path. Anat. **170**:426, 1903.

2. Weed, L. H.: The Cells of the Arachnoid, Bull. Johns Hopkins Hosp. **31**: 343, 1920.

3. Cushing, H., and Weed, L. H.: Studies on the Cerebrospinal Fluid and Its Pathway: IX. Calcareous and Osseous Deposits in the Arachnoidea, Bull. Johns Hopkins Hosp. **26**:367, 1915.

4. Mallory, F. B.: The Type Cell of the So-Called Dural Endothelioma, J. M. Research **41**:349, 1920.

5. Van Wagenen, W. P.: Elastic Tissue in Meningeal Fibroblastoma, So-Called "Dural Endotheliomas," Arch. Surg. **18**:1621 (April) 1929.

6. Penfield, W. G.: Cranial and Intracranial Endotheliomata-Hemicranosis, Surg., Gynec. & Obst. **26**:657, 1923.

They are of fairly frequent occurrence. Cushing,[7] in a series of 748 verified cases of brain tumor, reported 80 cases (10.7 per cent) of dural endotheliomas.

The relationship of these tumors to the skull is of interest. Cushing, in the aforementioned report, stated that twenty of his cases of dural endothelioma (25 per cent) were accompanied by a recognizable thickening of the overlying bone. He stated that the flat endotheliomas are more likely to provoke bony proliferation. According to him, the invasion of the bone canaliculi by tumor cells stimulates osteoblastic proliferation and subsequent hyperostosis. He also spoke of cases in which the bone is thinned or eroded, but gave no data as to the frequency of these cases.

Penfield[6] reported eleven cases from the literature and ten from his own studies, in all of which the patient gave a history of a gradually increasing lump over the cranial vault. In four of the cases from the literature microscopic examination showed actual infiltration of the bone by the tumor. From his own observations Penfield concluded that these tumors rarely or never penetrate the pia, and that they do infiltrate the overlying skull and scalp with bony proliferation. He stated that there is first rarefaction of the overlying bone and then stimulation of new bone formation. Endothelioma cells fill up the haversian systems, and there is a pad of endothelioma at the apex of the tumor just beneath the scalp. At this point the greatest osteogenic activity is found.

Phemister[8] reported three cases, two with localized hyperostosis and one with localized bone erosion and a little associated new bone formation. Barling and Leith[9] reported a case of a tumor arising in the pia-arachnoid and penetrating the dura to invade the overlying bone. There was marked osteoporosis but no attempt at new bone formation. The pathologic report was sarcoma of the endotheliomatous type, but the description and figures were those of a typical dural endothelioma.

Kolodny[10] studied ten cases of dural endothelioma, all with attached bony thickening. He explained the bony proliferation on the basis of local dilatation of the vascular channels of the skull, in turn due to growth of the underlying tumor mass, causing their stasis. Later invasion of the bone by tumor cells leads to bone destruction and

7. Cushing, H.: The Cranial Hyperostoses Produced by Meningeal Endotheliomas, Arch. Neurol. & Psychiat. **8**:139 (Aug.) 1922.

8. Phemister, D. B.: The Nature of Cranial Hyperostosis Overlying Endothelioma of the Meninges, Arch. Surg. **6**:554 (March) 1923.

9. Barling, H. G., and Leith, R. F. C.: Removal of a Cerebral Tumor (Endothelioma) Which Had Invaded the Overlying Cranial Bone, Lancet **2**:282, 1906.

10. Kolodny, A.: Cranial Changes Associated with Meningioma: "Dural Endothelioma," Surg., Gynec. & Obst. **48**:231, 1929.

occasionally to complete perforation of the skull. Taylor [11] reported a case in which the tumor was attached to the dura and had eroded the bone above it.

Thus, out of thirty-six cases (excluding Cushing's series) we have been able to find definite mention of only three cases in which there was definite destruction of the overlying bone.

The dural endotheliomas have usually been considered as benign tumors on the basis of the usual criteria. However, Taylor [12] cited from the literature two cases of dural tumor with metastases and three cases with invasion of the brain. The latter is unusual, as Hassin [13] and Hassin and Singer [14] have shown that in carcinoma of the cerebral meninges there is no invasion of brain tissue unless (as in one case that they reported) the subarachnoid space is so packed with tumor cells that the pressure forces them into the cerebral adventitial spaces. Even in such case only the superficial layers of the cerebral tissue are involved. Taylor considered the dural tumors as of low grade malignant character and characterized by slow spread, local malignancy and occasional metastases. Craig [15] presented a series of fifty-six cases of intracranial endotheliomas, eleven of which he considered malignant on the basis of absence of psammoma bodies, slight differentiation of cells and the presence of many mitotic figures. On the qualitative differences in the last two points he established a system of grading the malignancy.

We are presenting a case of intracranial tumor of long duration, originating from the dura, eroding the bone without any evidence of bony proliferation and bearing close microscopic resemblance to a malignant tumor.

REPORT OF A CASE

W. K., a man, 54 years of age, Polish, was admitted to the neurologic service (Dr. G. B. Hassin) of the Cook County Hospital on Jan. 31, 1930. He complained of numbness of the right extremities of three months' duration, weakness of the right extremities of one month's duration, a sensation of fulness in the head for two weeks, and an epileptiform attack on one occasion two days previous to admission.

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11. Taylor, W. J.: Report of a Case of Tumor of the Brain; Operation; Recovery; Death in 108 Days from Recurrence of the Disease, Am. J. M. Sc. **127**:287, 1904.

12. Taylor, J.: Invasion of the Skull by Dural Tumors, Brit. J. Surg. **16**:6, 1928.

13. Hassin, G. B.: Histopathology of Carcinoma of the Cerebral Meninges, Arch. Neurol. & Psychiat. **1**:705 (June) 1919.

14. Hassin, G. B., and Singer, H. D.: Histopathology of Cerebral Carcinoma, Arch. Neurol. & Psychiat. **8**:155 (Aug.) 1922.

15. Craig, W. M.: Malignant Intracranial Endothelioma, Surg., Gynec. & Obst. **45**:760, 1927.

He stated that he had been perfectly well until three months previously when, while at work, he was walking through a low door and, straightening up too soon, struck the vertex of his head severely against the top of the door. He did not fall or become unconscious at that time or later. There was no bleeding at any of the orifices nor was there any laceration of the scalp. A swelling in the left frontoparietal region was noted by the examiner and ascribed by the patient to a childhood injury thirty-five years previously. He stated that it had remained constant in size and had given no symptoms during all that time. Since his injury, three months previously, he stated that his right arm and leg felt numb, as though they were "asleep." Weakness of the right extremities had been present for one month and was more marked in the lower one. At the time of admission the patient felt that his right arm was improving. For two weeks a feeling of pressure, described as a "sensation of fulness," had been present intermittently in the left frontal region. Two days before admission the patient was sleeping at night and awoke at 1 a. m. About an hour later he had a convulsive attack consisting of "jerking" movements of the right arm and leg that lasted for about one minute. There was no aura, he did not cry out or lose consciousness, nor did he have bladder or rectal incontinence. He could not recall whether the attack began in the arm or in the leg. A similar attack of like duration occurred an hour later and he had had none since.

The patient was a laborer who had come to this country in 1914. He admitted the occasional use of alcohol, but stated that he had not used it for the past two months. His wife had had six children and no miscarriages, and he denied syphilitic infection. His past history and the family history were otherwise essentially unimportant.

General physical examination at the time of his admission revealed a well nourished, well developed, white man, about 50 years of age, who was not acutely ill. The temperature, pulse rate and respiration rate were normal, and the blood pressure was 138 systolic and 65 diastolic. There was a swelling in the left frontoparietal region, just to the left of the midline. This swelling was about the size of an English walnut, firm, nonfluctuant, firmly fixed to the skull and slightly tender. Pressure applied to the swelling caused no symptoms or subjective sensations. All the teeth were missing except the lower premolars and they were carious. There was a direct, reducible, incomplete, right inguinal hernia. The right testicle was atrophied, and there was a telangiectatic hemangioma on the dorsum of the left hand.

Neurologic examination revealed a slight spasticity of the gait, with a tendency to circumduction of the right lower extremity. The right arm was held motionless as the patient walked. The coordination tests were all satisfactorily performed with the exception of the finger to finger and right finger to nose tests which were done poorly. Muscle power was good in all the extremities and apparently equal. There was a slight increase in muscle tonus in the right lower extremity. The deep reflexes were moderately increased in the right lower extremity, and there was a sustained ankle clonus on the right side. The superficial reflexes were all present and equal, and there were no pathologic reflexes. All types of sensibility appeared to be normal, and there were no abnormalities of the cranial nerves. Examination of the fundi gave negative results.

The Kahn reaction of the blood was negative, the chemical composition of the blood essentially normal and the results of urinalysis essentially negative. Spinal puncture failed and the patient refused cisternal puncture. Roentgen examination of the skull revealed a defect near the midline, halfway between the lambdoid and coronal sutures. This defect was circular in outline and well defined, and there

was no evidence of associated bony proliferation. Unfortunate loss of the negatives prevents their reproduction. Roentgen examination of the long bones revealed no pathologic changes.

Dr. Hassin examined the patient and considered the condition to be associated probably with the tumor of the left frontoparietal region. He considered this tumor to be most likely an endothelioma in spite of the history of long duration with no symptoms before three months previously. He recommended operation, and the patient was transferred to a surgical service (Dr. George G. Davis) on February 20. His status had remained unchanged while he was on the neurologic service.

One of us (Dr. Davis) operated on the patient on March 10. A tumor mass, well defined, about the size of a plum and firm in consistency, was found adherent to the dura and extending through the eroded area of the skull. This tumor was

Fig. 1.—Dural endothelioma containing numerous whorls formed around hyaline masses of collagen fibrils. (Reproduced from Mallory: Principles of Pathological Histology.)

removed and sent to the pathologic laboratory for histologic examination. The report of the laboratory was that it was a squamous cell carcinoma, apparently metastatic.

The patient made an uneventful recovery from the operation. Thirteen days after the operation, neurologic examination revealed a definite weakness of both right extremities, a typical hemiplegic gait and a right foot drop. The deep reflexes were increased on the right side; there was a sustained ankle clonus on the right side, with a positive Babinski sign. The patient was transferred back to the neurologic service on March 23.

The laboratory report on the tissue removed led to further questioning of the patient and careful reexamination, neither of which yielded any clue as to the possible presence or location of a primary carcinoma. The patient's condition failed to improve, and he occasionally had an epileptiform seizure involving the right extremities. He was transferred to the county infirmary on June 4. He left this institution on August 14, in approximately the same condition as on admission, still alive, in good general health and with his hemiplegia slightly improved.

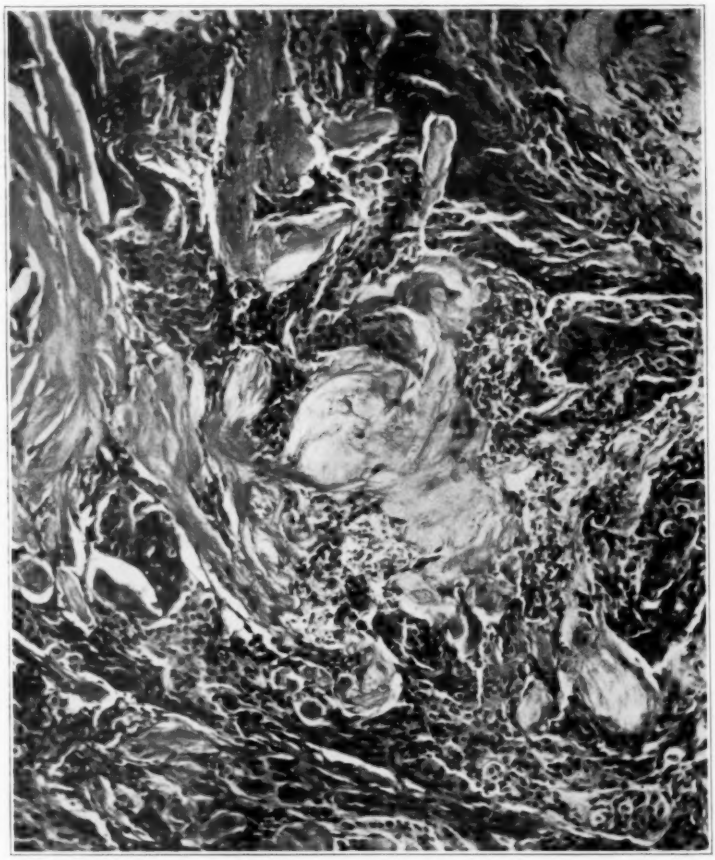

Fig. 2.—Photomicrograph showing avascular cell masses in a stroma of hyaline connective tissue; × 80.

The history of long duration of this tumor, the failure to discover any primary carcinomatous focus and the fact that the patient continued to remain in good physical condition all spoke against the original histologic diagnosis of the tumor. Hence one of us (Dr. Voris) reexamined the microscopic sections under the direction of Dr. Hassin with the aid of additional sections stained by the van Gieson technic. In addition Dr. Hassin has loaned us a section of carcinoma of the dura, a

photomicrograph of which we here reproduce (fig. 4) together with photomicrographs of our own (figs. 2 and 3).

The latter sections were stained both with hematoxylin and eosin (fig. 2) and also by the van Gieson method (fig. 3). They contained many avascular masses of deeply staining epithelial cells. In the van Gieson preparations these cell masses often contained pink staining

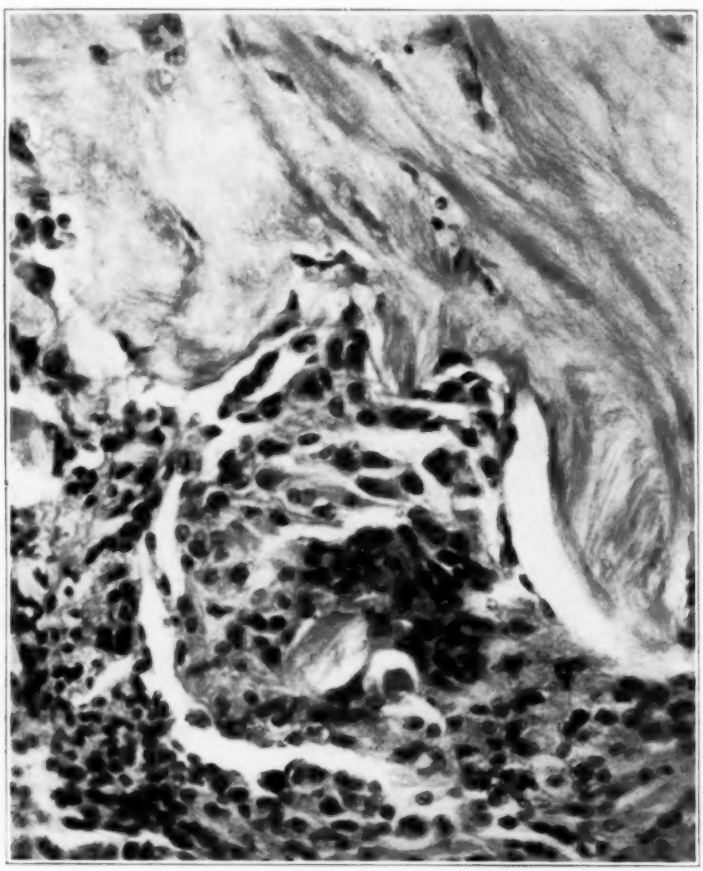

Fig. 3.—Same tissue as in figure 2; × 275.

fibers made up of many fine fibrils. At times these cell masses presented well defined borders, and at times the cells were arranged more or less in the form of whorls. There was no limiting membrane around the cell masses, and the cells often extended diffusely into the surrounding tissue and at times infiltrated it. In many of their nuclei there was a small dark nucleolus. No mitotic figures could be made out although the chromatin granules were excellently stained. In the center of

the larger cell masses many of the nuclei were shrunken, irregular, very deeply stained and occasionally even fragmented.

These cell masses were located in a stroma of pink staining, homogeneous, hyaline fibers which appeared slightly granular in the hematoxylin and eosin preparations and showed marked fibrillar structure in the van Gieson preparations. Many fibroblasts were scattered among

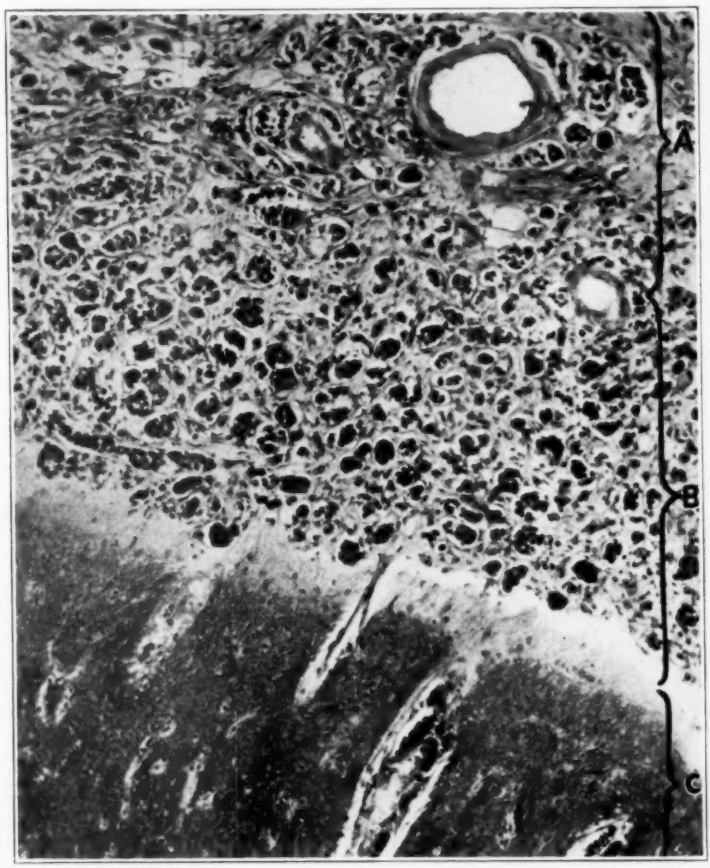

Fig. 4.—Photomicrograph of a metastatic carcinoma of the dura invading the underlying brain tissue: *A*, dura; *B*, leptomeninges and subarachnoid space, and *C*, brain; × 80.

these fibers, and in certain areas there were the infiltrating strands of the epithelial cells mentioned. In certain areas the fibers were much shrunken, sometimes fragmented, or even broken into small granules. These areas were much more lightly stained. The fibroblasts in these areas had their cytoplasm shrunken or entirely absent, and the nuclei were also shrunken, irregular in outline, deeply stained and, at times,

fragmented. In and around these areas blood cells were frequently present in small masses free in the interstices between the fibers. Blood vessels were generally absent from these areas and were few in number everywhere. Many of the blood vessels had their walls greatly thickened, and at times the lumen was almost occluded. These thickened walls presented a uniform homogeneous pink staining appearance.

For comparison with our material we are reproducing (fig. 1) a drawing of a typical dural endothelioma taken from Mallory's Principles of Pathological Histology.[16] This illustrates well the tendency of the typical dural endothelioma to form whorls of cells around hyaline masses of collagen fibers.

In figure 4 we present a photomicrograph of an unquestionable metastatic carcinoma of the cerebral meninges which was loaned to us by Dr. Hassin. The upper part of the picture represents the meninges infiltrated with numerous foci of carcinomatous cells; the lower part is the brain. Some vessels here show perivascular infiltrations with carcinomatous cells. The dura occupies the uppermost part of the picture. Attention should be called to the lack of reaction on the part of the connective tissue stroma, to the foci of small deeply staining cells and to the tendency of the latter cells to extend into the perivascular spaces of the underlying cerebral blood vessels. But this last occurs only when, as in this case, the subarachnoid space is very densely infiltrated with carcinoma cells. The gross appearance of this tumor is strikingly different from that of our tumor. It presents the appearance of multiple plaques infiltrating the dura overlying the brain. On the other hand, our tumor was a circumscribed mass definitely attached to the dura but not infiltrating it.

COMMENT

The following possibilities are present in this case. It may be, as first reported, a squamous cell metastatic carcinoma; it may be a dural endothelioma or meningioma, or finally, it may be a dural endothelioma of malignant character. Against the first possibility, that of a metastatic carcinoma, are the failure to discover a primary carcinomatous focus, the history of long duration before symptoms set in, the final slow onset, the single lesion, the failure to discover mitotic figures, the lack of symptoms of increased intracranial pressure and the present good general condition of the patient. Globus and Salinsky[17] reported twelve cases of metastatic tumor of the brain and stated that they were characterized by acute or precipitate onset, symptoms of increased intra-

16. Mallory, F. B.: Principles of Pathological Histology, Philadelphia, W. B. Saunders Company, 1914

17. Globus, J. H., and Salinsky, H.: Metastatic Tumors of the Brain, Arch. Neurol. & Psychiat. **17**:481 (April) 1927.

cranial pressure out of proportion to the neurologic observations, occasional signs of meningeal irritation, occasional pleocytosis and a rapidly declining clinical course.

The tendency of the epithelial cells to infiltrate the surrounding stroma in certain areas might speak for a low grade malignancy. Against this are the extremely slow growth of the tumor, the absence of mitotic figures and the absence of metastases.

The general structure of the tumor, the minute features already mentioned, the clinical course and the present good condition of the patient all point, it seems to us, to the diagnosis of endothelioma of the dura.

SUMMARY

A case of endothelioma (meningioma) of the dura is presented. The tumor was of thirty-five years' duration with symptoms only during the three months previous to the patient's admission to the hospital. It had eroded the skull, with no attempt at new bone formation. Pressure on the tumor gave no symptoms or subjective sensations. Operative removal aggravated the symptoms with gradual improvement and a residual hemiplegia. Microscopically, the structure of the tumor was that of an atypical endothelioma of the dura with slight evidence of low grade malignancy.

HISTOLOGY OF HEALING FRACTURES IN RATS ON NORMAL DIETS

W. G. DOWNS, JR., D.D.S., PH.D.
CHICAGO
AND
RAY M. McKEOWN, M.D.
Davis and Geck Fellow in Surgery
NEW HAVEN, CONN.

Our understanding of the problems of bone development and growth draws on many fields of scientific endeavor in order to build up a complete philosophy of the subject. A purely anatomic and histologic approach, while extremely valuable and for many years our only method of attacking the subject, gave us but a very incomplete picture of the natural history of bone. Tissue cultures, when added to the already existing data furnished by ground and decalcified sections, carried forward our appreciation of this complex subject.

Now, more recently, we have been enabled to add to our previous information that gained by studies on the physical structure and chemical composition of bone, and are well on the way to a more comprehensive understanding of osseous tissue than we possessed before. On the basis of our newer knowledge, it becomes necessary to revise somewhat the older views of bone physiology and pathology.

In a rather comprehensive series of studies on the breaking strength of healing fractured fibulae in rats on various synthetic diets reported by Lindsay and Howes [1] and later by McKeown, Lindsay, Harvey and Lumsden,[2] it was decided to study the histology of the changes involved in the healing of these fractured bones. It was felt that a correlation between the observed callus strength and the histologic picture could be obtained and that from this the special cell types responsible for the differences in strength from time period to time period throughout the course of the experiment could be determined.

To control future results on unbalanced diets, the animals were first placed on a standard or normal diet for one week and the right

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From the Department of Pathology and Department of Surgery, Yale Medical School.

The expenses of this investigation were defrayed in part by Davis & Geck, Inc.

1. Lindsay, M. K., and Howes, Edward: The Breaking Strength of Healing Fractures, I., J. Bone & Joint Surg. **13**:491 (July) 1931.

2. McKeown, R. M.; Lindsay, M. K.; Harvey, S. C., and Lumsden, R.: The Breaking Strength of Fractured Fibulae of Rats: II. Observations on a Standard Diet, Arch. Surg. **24**:458 (March) 1932; other papers in this series will follow in succeeding issues of the ARCHIVES OF SURGERY.

fibula was then fractured in the manner described by the aforementioned authors.[3] Two of the normal diet animals with fractured right fibulae were killed on each of the following postoperative time periods: six, twelve, eighteen and twenty-four hours. Two animals were also killed one, two, three, four, five and six days after operation, and at three day intervals thereafter.

The legs were then removed, and the tibiae and fibulae cleaned of all adhering soft tissues. These bones were fixed at once in 10 per cent formaldehyde, washed and embedded in celloidin, and that portion of the fibula containing the fracture was then sectioned longitudinally, and stained with hematoxylin and eosin, Mallory's connective tissue stain or Masson's triple stain. By sectioning the diaphysis longitudinally, a complete picture of the fracture at different levels was obtained.

Professor Maximow expressed his views on the subject of connective tissue growth through his "unitarian" theory.[4] This teaches us that in addition to connective tissue cells arising from the primary mesenchymal cells of the embryo, there is the greatest plasticity in the interchange of these cell types, occurring later in their life cycle. Fibroblasts may differentiate under proper conditions into chondroblasts or chondrocytes, into fat cells or the cells of the elastic tissues and, of particular interest for our purpose at present, into osteoblasts, osteocytes and probably these in turn into the so-called osteoclasts. Further than this, under proper conditions cells of the lymphocytic series, always present in the tissues, may revert to fibroblasts and hence on up to mature and further differentiated types of connective tissue cells.

It is through such studies as those of Maximow and of Häggqvist[5] that our knowledge of fundamental biologic processes has been built up. Häggqvist has had the courage to question the older views, and the energy to demonstrate that the conception of the osteoblasts having some peculiar quality that enables them, like glandular structures, to lay down calcium salts is probably not correct. He further believes that the osteoclasts are not in themselves responsible for the destruction of bone. He demonstrated that the osteoblasts are but the lineal descendants and successors of a rather long chain of connective tissue development, beginning, as Maximow also believed, with the mesenchymal cells, becoming next the fibroblasts and then, depending on whether the particular bone is to be membranous or endochondral,

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3. Lindsay and Howes (footnote 1). McKeown, Lindsay, Harvey and Lumsden (footnote 2).

4. Maximow, A., and Bloom, W.: A Textbook of Histology, Philadelphia, W. B. Saunders Company, 1930, pp. 48, 72 and 162.

5. Häggqvist, Gösta: Acta chir. Scandinav. **65**:180, 1929.

going directly into osteoblasts or, on the other hand, into chondroblasts, hence to chondrocytes and in turn to osteoblasts. As bone develops, these same cells become the osteocytes or the vital centers of the living, plastic bone. The osteoclasts, he considers, are but a residuum of protoplasm containing the clumped nuclei of osteocytes after the bone has been decalcified by purely chemical changes.

While these views are not accepted by all investigators without question, a careful study of our own material, in which a complete series of histologic preparations of the various stages of bone regeneration may be seen, tends to convince one that these theories, in at least their fundamentals, are correct and acceptable.

HISTOLOGY

Immediately after fracture of the fibula, blood is poured out from the ruptured vessels both in the bone and immediately adjacent to it to form a blood clot surrounding the line of fracture and extending out into the surrounding soft tissues for a short distance. Within eighteen hours, this has changed into a largely fibrinous clot with many lymphocytes present, but only the shadows of the erythrocytes. At the forty-eight hour period, this clot has become a well defined and outlined callus, made up entirely of fibrin and lymphocytes, and fairly well uniting the two fractured ends within the body of the callus. At this stage, the periosteum and endosteum have become "swollen" appearing and the individual cells may be made out with ease.

On the third day the periosteal and endosteal cells have begun to proliferate, and the lymphocytes within the clot are beginning to be replaced by young fibroblasts, apparently by metaplasia of these cells.

On the fourth day the callus has become entirely fibroblastic connective tissue—continuous with periosteum and the endosteum—completely filling the marrow cavity for some distance in each direction from the fracture line, and showing some tendency toward distinct condensation just across the line of fracture. An occasional large multinucleated cell may be seen along the margins of the still partly calcified trabeculae within the bone marrow and near the cortex. These are the cells commonly spoken of as osteoclasts.

On the fifth day there is further condensation of the fibrous callus through the line of fracture. There is a beginning of proliferation of small vessels and capillaries, and around these capillary buds may be seen irregularly deposited calcium salts. Also at this period many of the fibroblasts out in the body of the callus begin to have a rounded, "swollen" appearance. These are young chondroblasts. This is especially notable near the periphery of the line of fracture. The nuclei

Fig. 1.—Fifth day: fibrous callus, showing fragments of bone being cast off from fractured end. Hematoxylin and eosin; × 80.

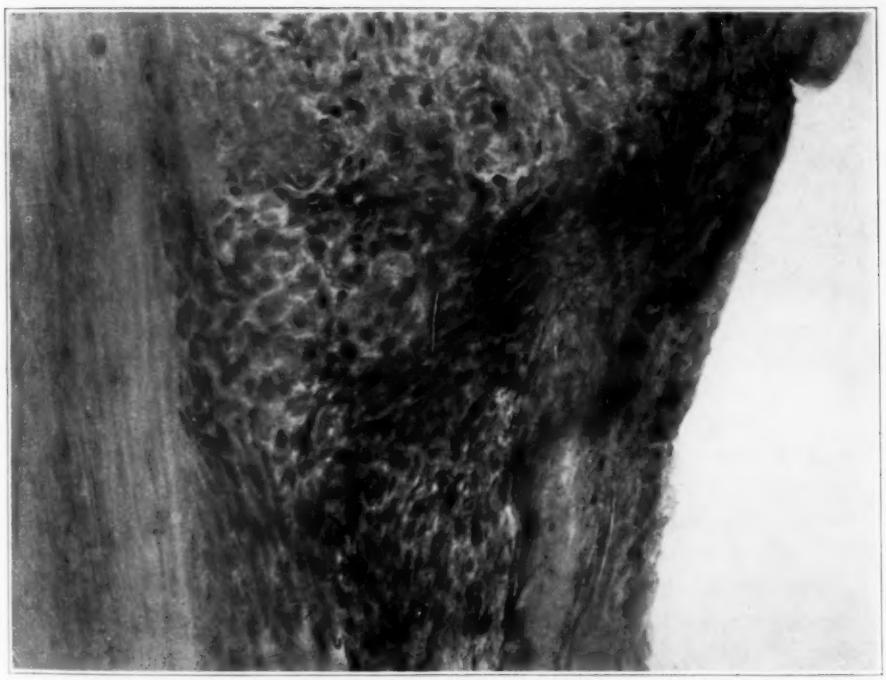

Fig. 2.—Fifth day: fibrous callus in region of proliferating periosteum, showing the "swollen" rounded appearance of the older of these cells. Hematoxylin and eosin; × 300.

of the osteocytes in the cortex and trabeculae begin, at this stage, to have a hyperchromatic appearance, and one may begin to see fragmentation of the bone near the fractured end (figs. 1 and 2).

On the sixth day the condensation of the fibroblasts directly in the fracture line and at the periphery, continuous with the periosteum, is more apparent. The large swollen cells near the periphery have begun to show hyperchromatic nuclei and have the appearance of cartilage cells. The infiltration of salts is more obvious and the calcifying areas are more extensive. A greater number of smaller fragments of bone

Fig. 3.—Sixth day: large clumps of swollen, rounded fibroblasts or chondroblasts. Many are now definitely seen to be chondrocytes. Hematoxylin and eosin; × 125.

may be seen, and the callus is much more highly vascular. More of the fibroblasts have the swollen appearance, while those at the center of such clumps have definitely taken on the characteristics of chondrocytes, and a few are definitely larger and hypertrophic (fig. 3).

On the ninth day the entire callus has become quite vascular, and the deposition of calcium salts forms an irregular network surrounding the capillaries. The masses of cartilage cells have become quite extensive, forming a plate through the line of fracture with a quite thick

mass or ring just inside the periphery of the callus. Many transitional stages between fibroblasts and chondrocytes may be seen at the periphery of this mass, and large clumps of hypertrophic chondrocytes are present. Only very rare bone fragments may now be detected and the cortex is receding from the line of fracture. Clumped around these ends are numerous large multinucleated cells (osteoclasts) (fig. 4).

On the twelfth day there is well marked organization of the callus. The mass of cartilage is larger, the calcifying network is more clearly

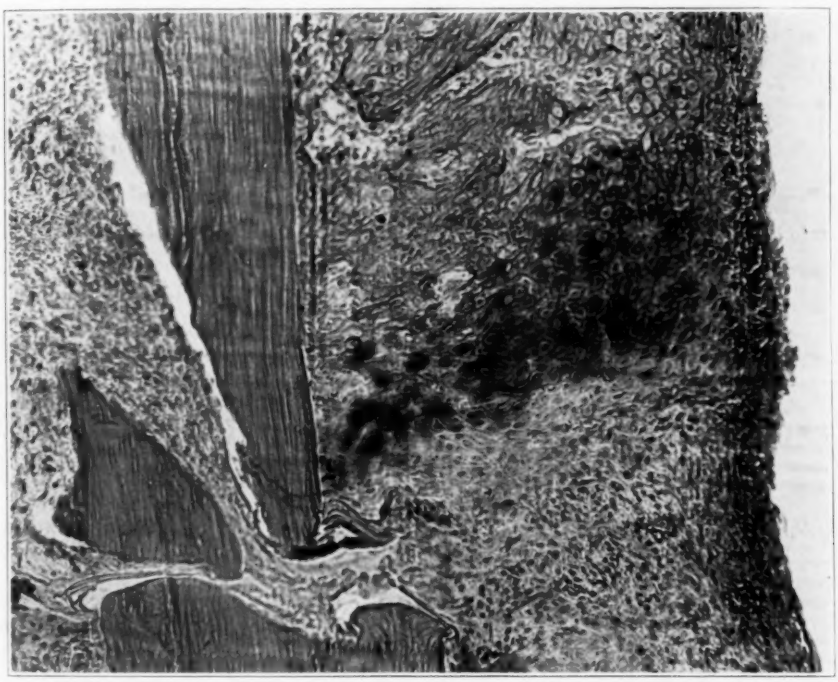

Fig. 4.—Ninth day: clump of chondrocytes; those at the center are becoming hyperplastic. In the upper part of the illustration the vascularity and depositions of calcium may be seen.

defined, and outside of the cartilaginous zone the vascular network is quite complete. There is, however, still no regularity in the pattern formed by any of these elements, nor are they joined across the line of fracture.

On the fifteenth day the calcifying strands have increased in size and density. The trabeculae are beginning to be more numerous near the cortex of the fractured end. The chondrocytes are beginning to line up in a fashion similar to that seen in epiphyseal growth in the

young animal. The chondrocytes are more numerous than at any later stage, and a very large number of them are hypertrophic. Osteoblasts are beginning to appear along the edges of the trabeculae, and the marrow cavity is beginning to extend into the callus (fig. 5).

On the eighteenth day the chondrocytes are in rather regular alinement with the calcified strands extending from the irregular network into the lines of deposition between the columns of cartilage cells. The network is everywhere continuous with the cortex and fills out all of the callus with the exception of the very central zone, made up of the

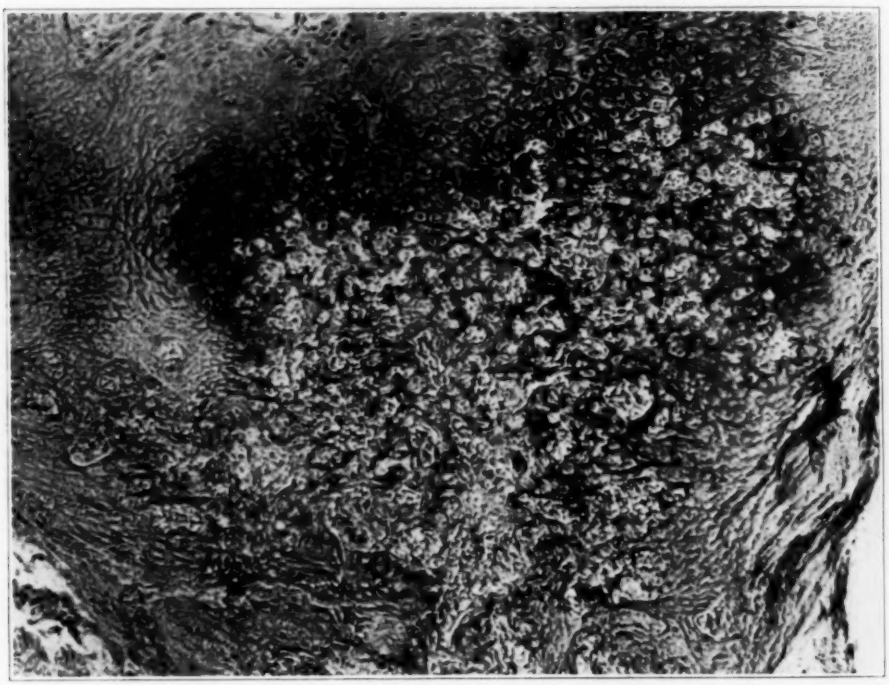

Fig. 5.—Fifteenth day: large mass of cartilage cells, most of which are at this stage swollen and hyperchromatic. At the periphery of this clump the forming trabeculae may be seen. Hematoxylin and eosin; × 125.

columns of cartilage cells. Many osteoblasts and a few osteoclasts may be seen with numerous transitional forms between the chondrocytes and these bone elements.

On the twenty-first day the entire callus is a mass of irregularly calcified trabeculae with, here and there between, small clumps of hypertrophic cartilage cells, containing hyperchromatic nuclei. The cortex proper has been resorbed quite far back from the line of fracture, and the network of the trabeculae seems to be continuous with the

"flared" end of this cortex. The entire callus has begun to shrink in size and the cartilage cells to decrease in number, and into the spaces between the trabeculae farthest from the fracture line, normal bone marrow cells are beginning to appear. At the fracture site there is still a dense, close, calcified network inclosing some hypertrophic cartilage cells (fig. 6).

On the twenty-fourth day there is marked encroachment of, first, capillaries and, behind that, bone marrow toward the line of fracture.

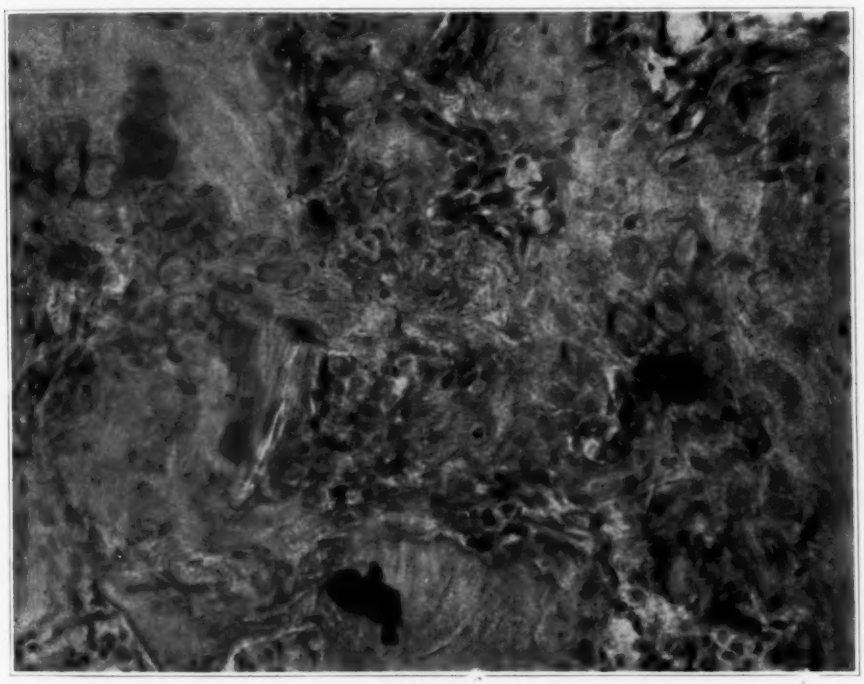

Fig. 6.—Twenty-first day: irregular mass of forming trabeculae, with stages between hypertrophic chondrocytes and osteoblasts apparent. Hematoxylin and eosin; × 300.

There is a marked decrease in the diameter of the callus with an increase in the size and density of the trabeculae.

On the twenty-seventh day the newly formed trabecular network completely joins across the line of fracture, with the chondrocytes almost entirely gone. The trabeculae are beginning to fuse near the periphery and farthest from the line of fracture.

On the thirtieth day the trabeculae across the fracture line are more marked, and practically all of the spaces contain essentially normal bone

marrow cells. The edges of the trabeculae contain many osteoblasts and osteoclasts, the result of the rapid changes of ossification.

On the thirty-third day there is a marked increase in the size of the newly formed marrow spaces near the center of the healing bone, with a decrease in their size near the periphery. Coincident with this, there is an increase in the number, size and density of the trabeculae near the periphery and directly continuous with the old cortex, and a complementary decrease nearer the center where the larger marrow spaces are to be found.

Fig. 7.—Thirty-sixth day: massing of trabeculae to form the new cortex. The medullary cavity is not yet complete. The new cortex is highly cellular and vascular. Hematoxylin and eosin; × 125.

On the thirty-sixth day these processes are continuous. There is, by this time, an almost complete new cortex, thicker, less dense than in the older portion and with the osteocytes large, hyperchromatic and in many loci apparently syncytial (fig. 7).

On the thirty-ninth day the marrow cavity is practically continuous through the site of the fracture. There is only a slight bulge to mark the site of the old cavity, and the cortex is still slightly thicker and contains numerous hyperchromatic osteocytes.

On the forty-second day the changes are still proceeding toward the preoperative conditions. Only an occasional incomplete trabecula may be seen in the medullary cavity. The cortex is only slightly thicker and less dense than is the case away from the line of fracture.

From the forty-fifth to the fifty-first day no particularly notable changes may be seen. On the fifty-first day, aside from a slight irregularity in outline, no difference may be seen between the architecture and histology at the old fracture site and elsewhere along the shaft of the bone (fig. 8).

Fig. 8.—Forty-fifth day: marrow cavity reestablished, cortex practically complete, less cellular, less vascular. Normal contour and thickness are almost obtained. Hematoxylin and eosin; × 125.

COMMENT

Bast [6] gave an excellent and detailed account of the histologic processes involved in bone repair in rabbits. Our study does not agree in all respects with his, particularly in that the entire series of changes observed by him had taken place with greater rapidity than was the case with our animals. It is felt, however, that the difference in species

6. Bast, T. H., and Sullivan, W. E.: Anat. Rec. **31**:255, 1925.

of animals and the entirely different methods of attack on the problem accounts for the lack of complete agreement in results.

Our own histologic studies on the healing of fractured fibulae in rats on a standard, well balanced diet agree closely with the series of events described by Maximow and by Häggqvist. Immediately after fracture, the site of the lesion fills in with blood from the ruptured small vessels. This blood clot is replaced within a matter of hours by a fibrin clot containing numerous lymphocytes. Soon these are replaced in the preparation by fibroblasts, and the clot has become a fibrous connective tissue callus, continuous with both the endosteum and the periosteum of the two fractured ends. At first, a few of these fibroblasts at the periphery become chondroblasts. As these become more numerous, the fibrous callus is gradually replaced by a cartilaginous callus.

Coincident with these changes, the old cortex is beginning to break up, and these decalcifying fragments, surrounded by multinucleated clumps of protoplasm (osteoclasts), may be seen in the callus nearest the cortical ends. In succeeding preparations, these fragments become less and less numerous, until by the twelfth day they are no longer seen. Before this series of events is complete, the older cartilage cells (chondrocytes) are beginning to assume the appearance of osteoblasts, and very irregularly distributed and formed clumps of calcifying protoplasm appear throughout the callus. As these increase in size, they merge into each other, and by the time the callus is well filled in by calcified strands the process of resorption or medullation has begun and the so-called "osteoclasts" again are seen.

At the next stage the cortex has become continuous over the site of the fracture and the medullary cavity is likewise reunited. Soon the entire bone has returned to practically its original form. From this stage on, the changes that take place in the production of normal, adult bone probably are in operation in the direction of Wolff's law of function governing form.

As has been said, Häggqvist does not believe that the osteoclasts in themselves are responsible for bone resorption. He has further postulated that in this process some other phenomena are responsible for the resorption of the bone salts and that the so-called "osteoclasts" are but a small amount of protoplasm with the clumped nuclei of the osteocytes that have remained behind after resorption has taken place. In other words, they constitute a residuum of decalcified bone.

Up to this point, we can go with Häggqvist almost without reserve. He further believes, however, that these so-called "osteoclasts" probably have no phagocytic powers. This we believe is open to question. A fine definition is here needed to determine what may be classed as phagocytic bone cells. That the basic protoplasm of bone enters into the

protoplasm of these cells and is in turn given up again to the blood stream seems to be fairly evident. This process is perhaps not phagocytosis in the strictest sense of the word. That these cells do not have the power of breaking down matured calcified bone, of ingesting particles of calcified bone, in spite of Jordan's [7] views to the contrary, we feel convinced is the correct view.

Up to this point, we have been relying on the studies of purely morphologic anatomy and histology, and here we must confess that we arrive at a dead end in our reasoning. It is now, however, that the studies of Pond [8] in this direction have amply demonstrated that, while the laying down of the organic matrix of bone—the formation of the collagenous protoplasm—is the function of connective tissue metabolism, the actual calcification, the conversion of the organic calcium, phosphorus and other salts to their inorganic forms in mature calcified bone is a purely physicochemical process of crystallization of these salts into the collagenous matrix. This chemical process is probably wholly independent of the cellular make-up of the tissues except for the need for the laying down of the proper chemically constituted matrix.

In the studies made on the breaking strengths of the healing fractured fibulae, it was observed that the primary callus was formed by the fifteenth day, at which time the callus strength was at a high level. Subsequently strength was lost rapidly until the twenty-first day, which was attributed to the development of the medullary cavity. This was followed by a gradual return to normal strength on the forty-fifth day through cortical thickening and reorganization of the callus.

Our histologic studies indicate that by the fifteenth day, when strength was at its initial highest rise, the hypertrophic chondrocytes were present in large numbers and calcification advanced. In explanation of the calcification at this period, the work of Fell and Robison [9] on avian embryonic limb buds strongly indicates that the hypertrophic cartilage cells are the source of a phosphoric esterase, which they termed phosphatase. To this enzymotic substance, they attributed the hydrolysis of the organic phosphates to the inorganic form found in bone.

It is at least possible, from the histologic picture that we noted on the fifteenth day, that the chondrocytes, which are in a hypertrophic state, are elaborating an abundance of phosphatase with the result that the calcific state is at its optimum and the strength of the callus at the high point observed.

The sharp loss of strength found to occur between the fifteenth and twenty-first day necessitates careful study. In an interval of nine days,

7. Jordan, H. E.: Anat. Rec. **20**:281, 1921.
8. Pond, S. E.: Internat. J. Orthodontia **14**:369, 1928.
9. Fell, H. B., and Robison, R.: Biochem. J. **23**:767, 1929.

the strength diminishes roughly 40 per cent. This cannot be associated only with the fusing of the ingrowing blood vessels that were noted grossly, but, on the contrary, some chemical factor of considerable power has come into the field and destroyed the unity of the calcified mass. That this is a blood substance is apparent when we consider that the skeleton in general simultaneously shows a rapid loss in strength. The decalcifying ability of the parathyroid hormone has been clearly demonstrated by Aub and his co-workers [10] in the treatment for chronic plumbism, as well as by Jaffe and Bodansky [11] in the experimental production of osteitis fibrosa cystica. That this may be the substance responsible for weakening the strength of the callus we can only assume, but in the face of our present knowledge the hypothesis is at least attractive. The chondrocytes are apparently deleteriously affected by the activity of the decalcifying substance, for their nuclei show a definite hyperchromatosis. It is not entirely unreasonable, then, to assume that the tentative suggestion of Kay [12] that an antagonism exists between phosphatase and possibly the parathyroid hormone is highly probable. Whatever the strength-reducing factor may be, its activity rapidly diminishes after the twenty-first day. Subsequently the development of true bone proceeds at a uniform rate, to attain its end-point on the forty-fifth day.

As more and more studies on the skeletal system are made, the high degree of plasticity it possesses becomes increasingly obvious. Collip [13] may be said to have first indirectly called our attention to this, and the studies made on the breaking strength of bone have borne it out. Connective tissue forms an extremely labile and changeable tissue. However, in a sense we still remain in the dark as to the stimulus initiating the various cytologic steps that we have observed. The impulse we do not know. It may be an amino-acid formed at the fracture site or it may be merely a disturbed physicochemical balance, but whatever it is we believe that the next few years will see a decided advance in our knowledge of bone.

SUMMARY

The cytologic processes involved in the healing of fractured fibulae in rats reveal the fundamental soundness of the views of Maximow and of Häggqvist as to the inherent abilities of connective tissue cells to

10. Aub, J. C., and Hunter, D.: Quart. J. Med. **20**:123, 1927. Bauer, W.; Aub, J. C., and Abrecht, J.: J. Exper. Med. **49**:145, 1929.

11. Jaffe, H. L., and Bodansky, A.: J. Exper. Med. **52**:669, 1930.

12. Kay, H. D.: Personal communication to R. M. McKeown, 1931.

13. Collip, J. B., in The Harvey Lectures, 1925-1926, Baltimore, Williams and Wilkins Company, 1927. Collip, J. B.; Clark, E. P., and Scott, J. W.: J. Biol. Chem. **63**:439, 1925.

change from one type to another under proper stimulus. Further, one may see adequate evidence of the physicochemical processes involved in bone healing—if the preparations are studied with this in mind.

The healing of bone on standard diets reveals the process to be divisible into the following stages:

1. A fibrinous clot, lasting until about three days after fracture.

2. A fibrous clot or callus, beginning to replace the fibrinous clot at about the second day after fracture and lasting until about the twelfth day.

3. A cartilaginous callus, beginning at about the sixth day and lasting until about the twenty-seventh day.

4. A calcifying callus, beginning almost coincidently with the formation of hypertrophic cartilage, reaching its greatest mass density at about the fifteenth day and following very closely the development and recession of the cartilage mass.

5. Last, the stage of ossification, beginning about the twenty-first day, that is, overlapping the stage of calcification and following through the later changes in the hollowing out of the marrow cavity, the organization of the cortex and the remodeling of the reformed bone.

A positive correlation has been shown to exist between the cytologic picture and the breaking strength of the healing callus at different time periods from the inception of the fracture to the restitution of its normal histologic structure and strength.

A histologic control or base line is established for comparison with the changes found in the healing of fractured bones of animals on different types of unbalanced diets.

HISTOLOGY OF HEALING FRACTURES IN RATS ON DIETS LOW IN TOTAL SALT, CALCIUM AND PHOSPHORUS

WILLIAM G. DOWNS, JR., D.D.S., PH.D.
CHICAGO
AND
RAYMOND M. McKEOWN, M.D
Davis and Geck Fellow in Surgery
NEW HAVEN, CONN.

Previous reports by Lindsay and Howes,[1] McKeown, Lindsay, Harvey and Lumsden,[2] and Downs and McKeown[3] have dealt with the breaking strength and histology of fractured fibulae in rats on normal and synthetic diets. The present study deals similarly with variations observed microscopically in the fractured fibulae of these animals when the salt content of their diet was markedly altered.

METHOD

As in the previous studies, the animals were placed on the diet utilized for one week, at the expiration of which time the right fibula was fractured in the manner described before.[1] Two animals from each dietary group were killed at the following postoperative time periods: six, twelve, eighteen and twenty-four hours. Two animals were also killed one, two, three, four, five and six days postoperatively and thereafter at three day intervals to and including fifty-one days. After death the legs were removed, and the tibiae and fibulae cleaned of all adhering soft tissue, and the bones then fixed in a dilute solution of formaldehyde U. S. P., 1:10. After ten days' fixation, they were decalcified in a 5 per cent solution of nitric acid in the diluted solution of formaldehyde, washed and embedded in celloidin. Later that portion of the fibula containing the fracture was sectioned longitudinally and stained with hematoxylin and eosin, Mallory's connective tissue stain or Masson's triple stain. However, after familiarity with the material had been gained, simple hematoxylin-eosin stain was the one generally adhered to. By sectioning the diaphysis longitudinally, a complete picture of the fracture at different levels was obtained.

The expenses of this investigation were defrayed in part by Davis and Geck, Inc.

From the Department of Pathology and Department of Surgery, Yale Medical School.

1. Lindsay, M. K., and Howes, E. L.: The Breaking Strength of Healing Fractures, I, J. Bone & Joint Surg. **13**:491, 1931.

2. McKeown, R. M.; Lindsay, M. K.; Harvey, S. C., and Lumsden, R. W.: The Breaking Strength of Healing Fractured Fibulae of Rats, II, Arch. Surg. **24**: 458 (March) 1932; others to follow.

3. Downs, W. G., Jr., and McKeown, R. M.: The Histology of Healing Fractures in Rats on a Normal Diet, Arch. Surg., this issue, p. 94.

For this series of studies, the diet utilized was the standard diet developed by Moise and Smith,[4] with the salt content varied as outlined by Osborne and Mendel.[5]

On each of the three diets 100 mg. of dried yeast powder was fed every second day, and antiscorbutic rations were given in large quantities at frequent intervals. It will be noted that the basic diets were not lacking in vitamin content.

HISTOLOGY

There was little difference cytologically between the fractures of the "standard" or normal diet animals [3] and those on the various low salt

TABLE 1.—*Standard or Basic Diet*

	Per Cent	Calories per Kilogram of Food	Apportionment of Total Calories, per Cent	
Casein	18	738	Protein	13.8
Starch	51	2,091	Carbohydrate	39.2
Crisco	22	2,046		
Cod liver oil	5	465	Fat	47.0
Salts (varied according to the diet being fed)	4			
	100	5,340		100.0

TABLE 2.—*Salt Content of the Different Diets*

	Low Calcium Diet	Low Phosphorus Diet	Low Total Salt Diet
Calcium carbonate	0.00	12.24	No salt mixture whatsoever was added to the basic diet
Magnesium carbonate	2.42	1.21	
Sodium carbonate	5.80	1.71	
Potassium carbonate	14.13	3.53	
Orthophosphoric acid	3.72	0.00	
Hydrochloric acid	5.34	5.34	
Sulphuric acid	0.92	0.92	
Citric acid and water	11.11	9.50	
Ferric citrate, 1½ water	0.634	0.634	
Potassium	0.002	0.002	
Manganese sulphate	0.0079	0.0079	
Sodium fluoride	0.0248	0.0248	
Alum	0.00245	0.00245	
Lactose	246.00	246.00	

diets during the first six days postoperatively. Immediately following the fracture, a blood clot formed in and about the fractured bone. This changed within eighteen hours into a clot largely fibrinous in character in which many lymphocytes, but only the shadows of erythrocytes, were observed. By the end of forty-eight hours the clot had become a well defined callus made up entirely of fibrin and lymphocytes, uniting the fractured ends within its body. At this stage, the individual cells of the periosteum and endosteum could easily be seen. On the third day, the periosteal and endosteal cells were undergoing proliferation, and the lymphocytes within the clot were being replaced by young fibroblasts.

4. Moise, T. S., and Smith, A. H.: J. Exper. Med. **40**:13, 1924.

5. Osborne, T. B., and Mendel, L. B.: J. Biol. Chem. **34**:131, 1918; **37**:557, 1919.

On the fourth day, the callus consisted entirely of fibroblastic connective tissue continuous with the periosteum and the endosteum. It completely filled the marrow cavity for some distance in each direction from the fractured line, and showed a tendency to condense across the fracture gap. A few large multinucleated osteoclasts could be seen by this time along the margins of the still partially calcified trabeculae within the bone marrow and near the cortex. On the fifth day, there was further condensation in the fibrous callus through the path of the fracture. In addition it was observed that a proliferation of vessels and capillaries was occurring. It was further noted that in and around these capillary buds or tufts irregular depositions of calcium salts were developing. Simultaneously, many of the fibroblasts in the body of the callus increased in size and assumed a shape roughly spherical. These latter cells were young chondroblasts, and their number differed somewhat in the animals on the three diets studied. The presence of the chondroblasts was, in general, especially notable near the periphery of the line of fracture. The nuclei of the osteocytes in the cortex and trabeculae at this stage appeared slightly hyperchromatic, and it was seen that fragmentation and dissolution of the bone about these areas of hyperchromatosis was manifesting itself, particularly so in the distal end of the shaft of the fractured fibula. On the sixth day, the condensation of the fibroblasts directly in the midline of the fracture, as well as in its periphery, was continuous with the periosteum. It was also observed that, except in the animals on the diet low in calcium, young cartilage cells were beginning to appear in considerable numbers through the superior planes of the callus. From this stage on, the processes observed differed somewhat in the animals on the three types of diets studied and may be described to advantage as separate entities.

9 Days

Low Salt	Low Calcium	Low Phosphorus
Definite clumps of cartilage cells, none as yet hypertrophic, beginning of fibrous trabeculation, but with no calcification apparent; decalcification of ends of cortex	Callus largely dense fibrous connective tissues; no trabeculation; some fragmentation of cortex; few or no osteoclasts and no chondroblasts	Quite dense connective tissue callus; a few cells away from line of fracture and near periphery beginning to have "swollen" appearance and larger and hyperchromatic nuclei. Occasional chondroblasts seen

12 Days

Large clumps of cartilage, many cells hypertrophic; decalcification of cortex and of fragments but no calcification of fibrous trabeculae	Largely fibrous connective tissue; a few fibroblasts beginning to look swollen; a few osteoclasts at ends of cortex; beginning condensation into fibrous trabeculae	Chondrocytes are more numerous, especially near periphery and away from fracture line; network of dense fibrous connective tissue well formed except across fracture line

15 Days

Callus almost entirely hypertrophic cartilage; slight calcification of trabeculae; marked decalcification of fragments in cortex; no calcification of trabeculae or fibrous connective tissue aross fracture line (fig. 1)	Cartilage cells fairly numerous through fracture line especially; decalcification of cortical ends quite marked; further condensation of fibrous connective tissue trabeculae in which there is no evidence of calcification (fig. 2)	Chondrocytes and chondroblasts present in large masses near the fracture line, except in center; bony ends and fragments being rapidly absorbed; many multinucleated masses, osteoclasts present in this central region; no evidence of calcification (fig. 3)

Fig. 1.—Photomicrograph of fractured fibula of animal killed after fifteen days on a low salt diet, showing large amounts of cartilage, fibrous callus and decalcification of ends of cortex; × 75.

18 Days

Large numbers of hypertrophic cartilage cells irregularly arranged; no great change from fifteen day period	Further condensation of trabeculae, with little evidence of calcification; marrow cavity extending closer to line of fracture	Picture essentially unchanged, except that marrow cavity is beginning to encroach on masses of connective tissue and cartilage in fracture line

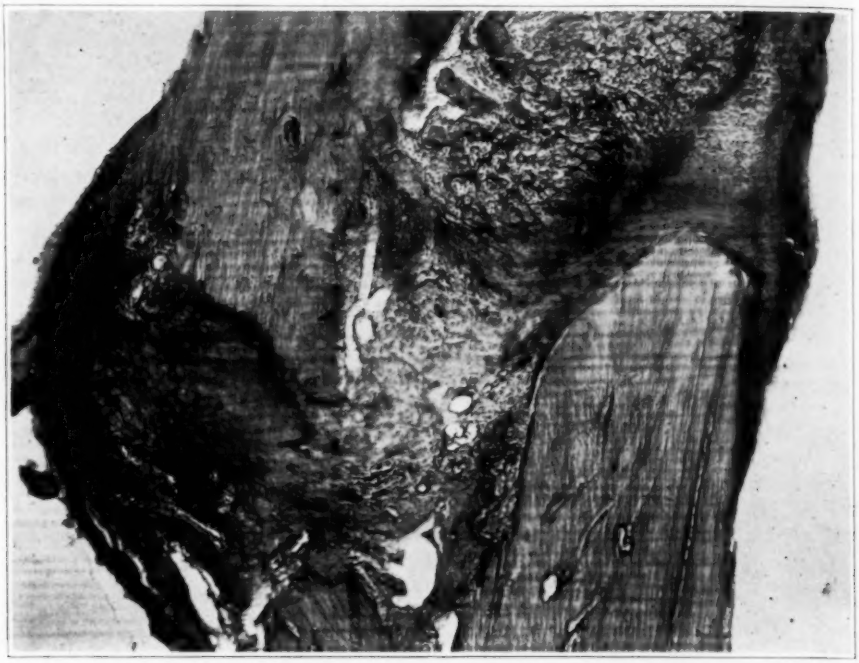

Fig. 2.—Photomicrograph of fractured fibula of animal killed after fifteen days on a low calcium diet, showing condensation of connective tissue callus, few cartilage cells and no evidence of calcification; × 75.

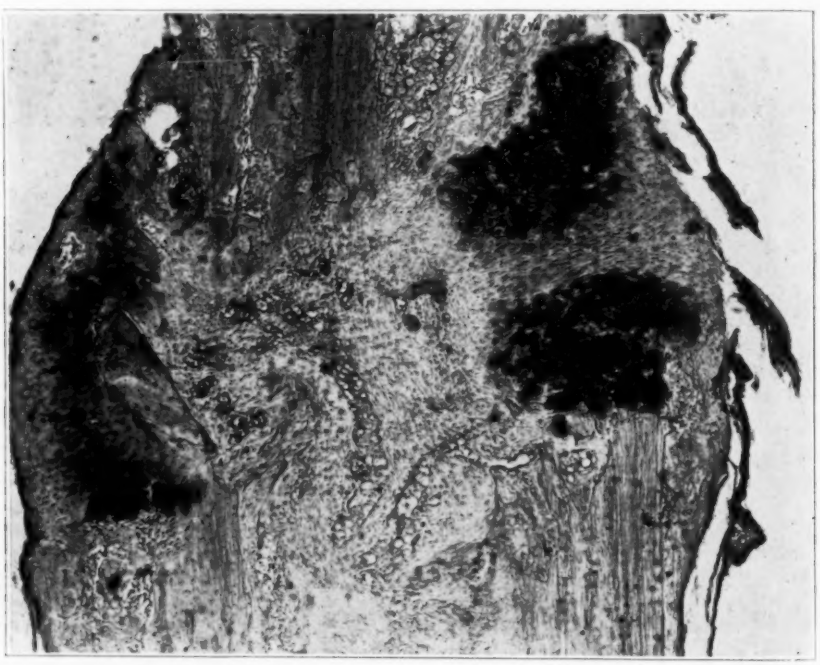

Fig. 3.—Photomicrograph of fractured fibulae of animal killed after fifteen days on a low phosphorus diet, showing large masses of chondroblasts and chondrocytes, especially near periphery of the line of fracture, and marked resorption of the cortex of the trabeculae; × 75.

21 Days

Less cartilage, some calcification of trabeculae which are invading cartilaginous mass at fracture line (fig. 4)	More condensation of trabeculae; distinct effort to form a thin cortex; not greatly calcified (fig. 5)	An almost complete disk of cartilage can be seen filling fracture line and extending each way up into marrow cavity and adjacent to bone marrow cells; very little fibrous connective tissue remains (fig. 6)

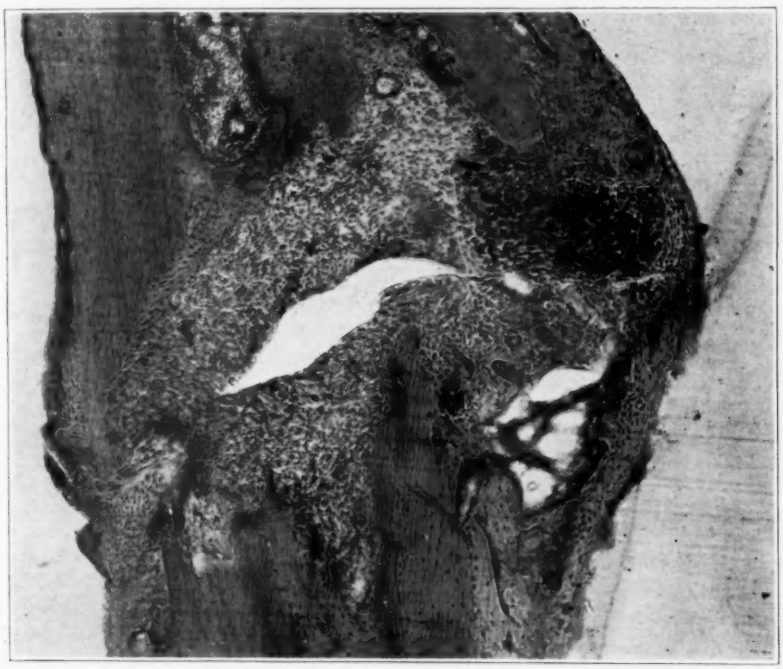

Fig. 4.—Photomicrograph at the twenty-one day period, low salt diet, showing only small amount of cartilage, fibrous trabeculae invading callus and some calcification of trabeculae; × 75.

24 Days

More trabeculae, only slightly calcified; considerable numbers of hypertrophic cartilage cells remaining	Uncalcified connective tissue cortex and trabeculae beginning to fuse across fracture line	Picture essentially unchanged; hypertrophic cartilage cells not conspicuous; little evidence of decalcification; none of calcification

27 Days

Many cartilage cells remaining; larger numbers of trabeculae; slight calcification	Still many cartilage cells in fracture line and near it; little evidence of calcification	Little change; cartilaginous disk still fills line of fracture; possible slight condensation of shaft

Fig. 5—Photomicrograph at the twenty-one day period, low calcium diet, showing condensation of trabeculae, formation of thin cortex and little or no calcification; × 75.

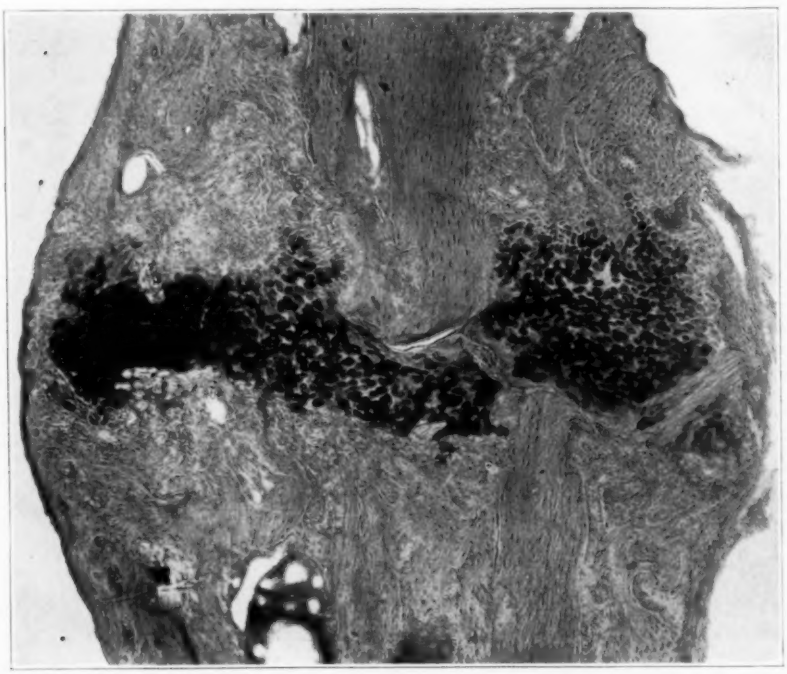

Fig. 6.—Photomicrograph at the twenty-one day period, low phosphorus diet, showing nearly complete disk of cartilage through line of fracture, little fibrous tissue present and trabeculae forming outside mass of cartilage; × 75.

30 Days

No marked change; trabeculae calcified up to mass of cartilage which still formed fracture line; this is making an effort to line up in a fashion similar to growth in the epiphyses of young bones	Little change; decalcification still obvious; further condensation of trabeculae, but little evidence of calcification	Slight changes only; in some places cells are apparently going back from cartilage to an earlier fibrous connective tissue type of cell

33 Days

No particular changes	Conditions little changed; slight evidence of calcification; cortex more complete across fracture line	Slight if any changes in fracture line; cortex slightly more dense and mature-appearing away from fracture line; cartilaginous disk still complete

36 Days

Some condensation of trabeculae at sides near cortex, but still little invasion of cartilaginous callus	Architecture nearly normal, but little evidence of calcification in newformed cortex and trabeculae; no cartilage to be seen	No appreciable changes from preceding period

39 Days

No marked change; greater condensation of trabeculae in cortex away from cartilaginous callus (fig. 7)	Essentially unchanged (fig. 8)	Disk of cartilage still apparent between fractured ends; slightly greater encroachment of dense connective tissue trabeculae into cartilage; picture very similar to that of epiphysis in marked rickets (fig. 9)

42 Days

Trabeculae have broken through the cartilaginous callus in line of fracture; some evidence of calcification of these trabeculae in cortex	Slightly more evidence of calcification; cortex very cellular; areolae around bone cells very large, and the cells themselves are also large and pale looking	Disk of cartilage thinner; connective tissue trabeculae encroaching into this disk; only slight evidence of calcification of these encroaching trabeculae

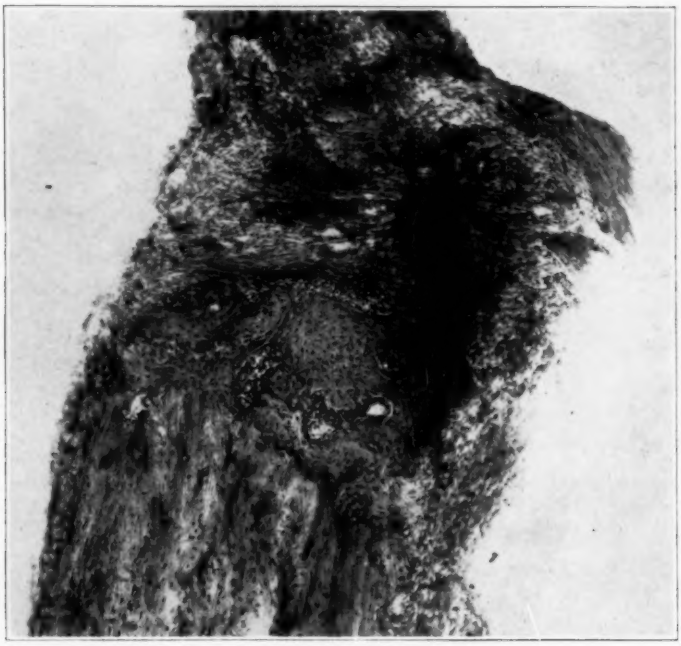

Fig. 7.—Photomicrograph at the thirty-nine day period, low salt diet, showing trabeculae condensed near fracture line, but much cartilage still present, and considerable calcification; × 75.

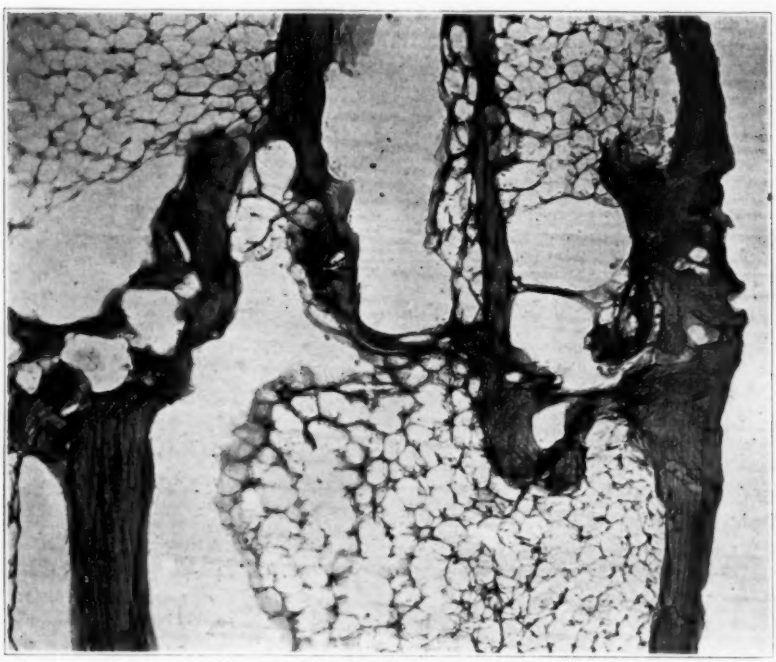

Fig. 8.—Photomicrograph at the thirty-nine day period, low calcium diet, showing architecture nearly restored, but very light and thin and poorly calcified, an absence of bone marrow cells in this region, and an irregular cortex; × 75.

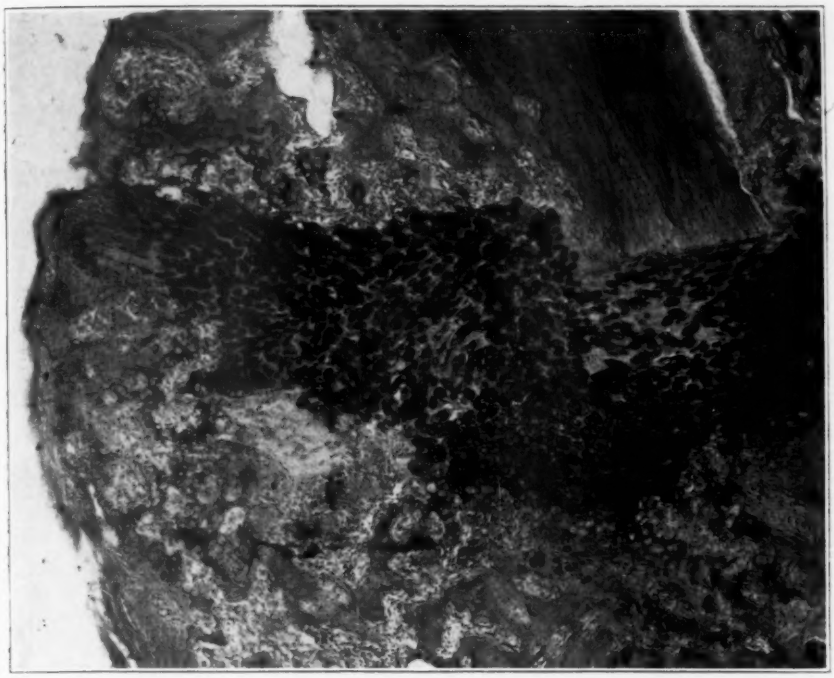

Fig. 9.—Photomicrograph at the thirty-nine day period, low phosphorus diet, showing complete disk of cartilage still apparent across fracture line giving a picture very similar to that of epiphyses in rickets; × 75.

Fig. 10.—Photomicrograph at the forty-five day period, low salt diet, showing cortex and trabeculae thick, but still quite cellular, definite calcification and the presence of bone marrow cells; × 75.

Fig. 11.—Photomicrograph at the forty-five day period, low calcium diet, showing architecture well restored, cortex not well differentiated, little calcification and no marrow cells; × 75.

Fig. 12.—Photomicrograph at the forty-five day period, low phosphorus diet, showing cartilaginous disk still not displaced with invasion by amorphous-looking connective tissue and no evidence of calcification in callus proper; × 75.

45 Days

Modelling or medulation beginning; cartilage nearly gone (fig. 10)	Cortex slightly thicker, denser, better calcified (fig. 11)	Cartilage being irregularly displaced by a rather amorphous looking mass of connective tissue; very slight evidence of calcification (fig. 12)

48 Days

Cortex thicker; trabeculae more massed; more advanced calcification	Essentially unchanged; cortex somewhat thicker, more complete; calcification still only slight	Marrow cavity partly extended through callus; cartilage cells can still be seen in the irregular cortex

51 Days

Architecture practically restored; cortex fragile but complete; only few remaining trabeculae; these and cortex highly cellular	Cortex at fracture line still not well calcified, quite cellular; achitecture essentially restored	Similar to 48 day period; marrow cavity somewhat larger; cortex slightly more dense and compact, still extremely cellular; a few chondrocytes can still be seen scattered through the callus

COMMENT

It is quite obvious from a study and analysis of this series of histologic preparations that changes in the healing fractures of animals on a low salt diet follow, in general, the changes described in fractures of rats on a standard diet,[3] but with a general retardation of the entire reparative process. However, marked variations are to be found in the fractured fibulae of animals on low calcium and low phosphorus diets. In the case of the animals on the low calcium diet, the outstanding picture is the general delay in the calcific processes. The cellular responses involved in the low calcium fractures are similar in order of appearance to those in the normal animals, but are again so retarded as to be almost absent until late in the healing reaction.

The cytologic response to a low phosphorus diet, on the other hand, is characteristic. Here cartilage formation begins at about the time that it is found in the animals on normal diets, but progresses much more rapidly to form a complete disk through the line of fracture, which apparently becomes a definite obstacle to the ingrowth of normal bone. More and more this cartilaginous disk simulates the picture seen in the rachitic epiphyses.

In work reported elsewhere,[6] it has been shown that the curve of the healing strength of fractured rat fibulae gains its first peak on the fifteenth day of healing, falls thereafter for six days, and subsequently gains an end point with strength nearly restored by the forty-fifth day. The strength of the healing fracture is largely, but by no means entirely, attendant on the extent of calcification of the callus, and it was with this that we were primarily concerned in the present studies.

Calcification of a fracture follows the development of cellular elements in the fracture, and apparently is the result of their activity. Fell and Robison [7] expressed the belief that hypertrophic cartilage cells, such as were found in our studies, are the precursors of an esterase-phosphatase, through the activity of which calcium phosphate compounds are precipitated. One of us [8] (Dr. McKeown) has been able to demonstrate in fractured rat fibulae that following fracture this esterase first increases locally and later decreases fully as rapidly as it rose. By the time the primary callus has formed on the fifteenth day the phosphatase content was diminished, and, with the sharp reduction in callus strength between the fifteenth and twenty-first days, phosphatase was restored to a level nearly that of normal. Later, as the callus strength again rose, eventually becoming equal to the normal, the phosphatase apparently varied but slightly.

It is somewhat difficult to conceive of phosphatase being a product entirely of cartilage cells, as Fell and Robison [7] suggested. If such were the case, phosphatase should be at its highest level after the fifteenth day, and the callus strength proportionately greater. Murray [9] is of the opinion that phosphatase is not the product of hypertrophic cartilage, but of the death of tissue cells. This is an attractive hypothesis and one that he has studied carefully, but tissue death is evidently not productive of the optimal alkaline hydrogen ion concentration, which we have found essential for the hydrolytic reaction of phosphatase; rather, it is apparently productive of an acidic state inhibitory to the phosphatase.

It would seem that the possibility expressed elsewhere that phosphatase is antagonized by parathyroid hormone is more attractive as a hypothesis.[2] The cartilage cells could form phosphatase, but at a certain stage the activity of the esterase would be inhibited by the hormone. The reason for the inhibitory state developing on or about the fifteenth day we do not know, but evidently it does so regardless of the diet or other treatment.

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6. Lindsay and Howes (footnote 1). McKeown, Lindsay, Harvey and Lumsden (footnote 2). Downs and McKeown (footnote 3).

7. Fell, H. B., and Robison, R.: Biochem. J. **23**:767, 1929

8. McKeown, R. M., and Ostergren, J. I.: Proc. Soc. Exper. Biol. & Med. **29**:54 (Oct.) 1931.

9. Murray, C. R.: Personal communication, 1931.

Callus strength was clearly lower than normal during the first fifteen days of healing. Thereafter it varied less. The histologic appearance of the different fractures varied more than did the healing strength. We were unable to demonstrate histologically any decided reduction in the number of cartilage cells in the fractures. If callus strength was less than normal during the first fifteen days, when we have shown phosphatase to be at its height, it is conceivable that, owing to a reduction in the diet of the substances on which phosphatase acts, callus strength might be reduced, and this, in itself, may explain the early variations from normal.

If the lowered strength during the first fifteen days is due to a lack of salt in the diet, it should follow that the strength was more reduced on the low total salt diet than on either the low phosphorus or the low calcium diets. This proves to be the case, as we have reported elsewhere. Further, the strength of the callus in its early stages would be more reduced on the calcium than on the low phosphorus diet if the calcium salts are more closely concerned in the strength of the callus than are phosphorus salts. This also proves to be true.[2] In the histology of the fractures of the animals on the low calcium diets, we were struck by the absence of calcification as compared with that appearing in the animals on the other two diets, and although the healing strength was not extremely reduced in the animals on the low calcium diet, it was definitely less than that in those on the low phosphorus diet.

SUMMARY

A histologic study of healing fractured fibulae of rats on low total salt, low calcium and low phosphorus diets has been made. There is some evidence of correlation between the histology and the breaking strength of these calluses, but the correlation is not as complete as could be desired. It is believed that further evidence of an indirect nature is presented on the importance of phosphatase to the healing of bone.

TUMORS OF THE SMALL INTESTINE

THEODORE S. RAIFORD, M.D.
Department of Surgery, Johns Hopkins Hospital
BALTIMORE

The subject of neoplastic growths occurring in the small intestine is a difficult one to approach in view of the paucity of material. The infrequency of gastro-intestinal tumors located between the pylorus and the ileocecal valve is one of the many unsolved problems of cancer pathology and it is interesting to speculate why this part of the alimentary canal is relatively immune to tumor invasion when the portals of entrance and exit, namely the stomach and the large intestine, are among the most common sites for cancer. Literature on this subject is not scarce, but the majority of publications in the past have dealt with case reports alone. Few authors have ventured to discuss the theories of causation and pathogenesis. A former paper (1931) dealt with the clinical aspects of tumors of the small intestine, special emphasis being laid on the diagnostic importance of the roentgen rays. The purpose of this article is to summarize the cases recorded in this hospital and to discuss the occurrence, the clinical features and the histopathology of the group.

Interest in small intestinal growths was aroused by the occurrence of two cases in the wards of the Johns Hopkins Hospital during the past year. Since that time three cases have been reported from other hospitals in Baltimore. A search of all available material then revealed eighty-eight cases of tumors of the small intestine. This material included 11,500 autopsies in the general pathological department and 45,000 specimens from the surgical pathological department, a large percentage of the latter including specimens sent from other hospitals for diagnosis.

The frequency of tumors of the small intestine can best be appreciated by a comparison with tumors occurring in the rest of the gastro-intestinal tract. Tables 1 and 2 illustrate this relation. It will be noted that tumors of all types occurring in the small intestine comprised 8.9 per cent of all gastro-intestinal tumors. Those of benign character are relatively more frequent in the small intestine, comprising 23.8 per cent of all benign tumors. Malignant tumors are, comparatively speaking, less common, occurring in only 4.9 per cent of all those in the gastro-

From the Surgical Pathological Laboratory of the Johns Hopkins Hospital and University.

intestinal tract. These values parallel closely figures quoted by other writers on the subject. Herman and von Glahn, considering malignant tumors alone, placed the incidence at 3.1 per cent. Ewing reported a value of 3 per cent; Forque and Chavin, reviewing 88,031 autopsies, placed the incidence at 6 per cent.

A thorough perusal of the literature yielded 339 tumors of the small intestine, the reports of which could be considered authentic. While

TABLE 1.—*Distribution of Nine Hundred and Eighty-Six Gastro-Intestinal Tumors*

Source		Cases From the Surgical Pathologic Department	Cases From the General Pathologic Department	Total
Stomach	Benign	0	58	58
	Malignant	263	190	453
	Total			511
Colon and rectum	Benign	51	36	87
	Malignant	190	91	281
	Total			368
Appendix	Benign	8	0	8
	Malignant	9	0	9
	Total			17
Small intestine	Benign	13	37	50
	Malignant	20	18	38
	Total			88
	Grand total			986

TABLE 2.—*Ratio of Tumors of the Small Intestine to Total Gastro-Intestinal Neoplasms*

All tumors		
Gastro-intestinal	986	
Small intestine	88	(8.9%)
Benign tumors		
Gastro-intestinal	210	
Small intestine	50	(23.8%)
Malignant tumors		
Gastro-intestinal	776	
Small intestine	38	(4.9%)

the number reported in the present series is relatively large, it must be remembered that all atypical growths, excluding infectious processes, were considered. The majority of these were asymptomatic and were recognized accidentally at autopsy.

The majority of writers have neglected to discuss the infrequency of this group of tumors from the etiologic standpoint, and while such neglect is perhaps justifiable in the present state of knowledge, there are certain characteristics in which the small bowel differs from the stomach and large intestine. These differences have to do with the

embryology, anatomy and physiology of this portion of the intestine, and therein may lie the basis of its insusceptibility to tumor invasion.

Summarized briefly, the small intestine is an epithelial-lined tube that has undergone rapid elongation in the embryo out of proportion to the rate of growth of the remainder of the gastro-intestinal tract. It is a coiled tube of relatively uniform size, the lining of which is characterized by villi between which lie the crypts of Lieberkuhn. The mucous glands of Brunner are found in the submucosa of the duodenum and upper jejunum, while the terminal ileum harbors collections of lymphoid tissue known as the agminate nodules or Peyer's patches. Food materials pass through the small intestine rapidly, with little or no stasis, save in the lower ileum. The absorptive power is greater in the small bowel than in any other portion of the intestinal tract, and it contributes the great majority of the secretions essential to

TABLE 3.—*Varieties and Location of Tumors of the Small Intestine*

Type	Duodenum	Jejunum	Ileum	Undetermined	Total
Carcinoma	7	4	3	2	16
Sarcoma	0	1	1	0	2
Lymphoblastoma	1	0	18	2	21
Adenoma	4	1	10	0	15
Myoma	0	1	2	0	3
Fibroma	1	0	3	0	4
Hemangioma	1	1	1	0	3
Chylangioma	0	1	0	0	1
Hematoma	0	0	1	1	2
Accessory pancreatic tissue	2	3	1	0	6
Argentaffin tumors	1	1	5	0	7
Lipoma	3	1	3	0	7
Cyst	1	0	0	0	1
Total	21	14	48	5	88

digestion in an alkaline medium. While it may seem impracticable to attempt to prove a relationship between these factors and the infrequency of neoplastic growth, they should receive due consideration.

The relative freedom from stasis of the small intestine should be regarded as significant. The terminal ileum is the only part of this field in which the fecal contents are brought to a standstill and accumulate before passing into the cecum. This is the region in which the tumors of this series are found to occur most frequently. Stasis likewise is found in the stomach and large intestine, and these sites are especially susceptible to tumor invasion. Stasis is known to be conducive to irritation, and if one accepts the irritation theory of the etiology of cancer, this must be accepted as a contributing factor.

The embryonic theory of Cohnheim has many supporters, and in certain cases it clearly accounts for tumor origin. If one bears in mind the fact that the small intestine develops chiefly during the latter four months of fetal life it is plausible to assume that there is far less opportunity for arrested development and misplaced embryonic tissue here than in the remainder of the gastro-intestinal tract.

The variety of tumors in this series and their distribution may be comprehended at a glance at table 3.

Tumors of the lymphoblastoma group, about which much confusion still exists and which will be taken up in detail later, were found to be most common, occurring in twenty-one instances. Eighteen were located in the ileum, the site of election being the terminal portion. Carcinomas were the next in frequency, accounting for sixteen of the

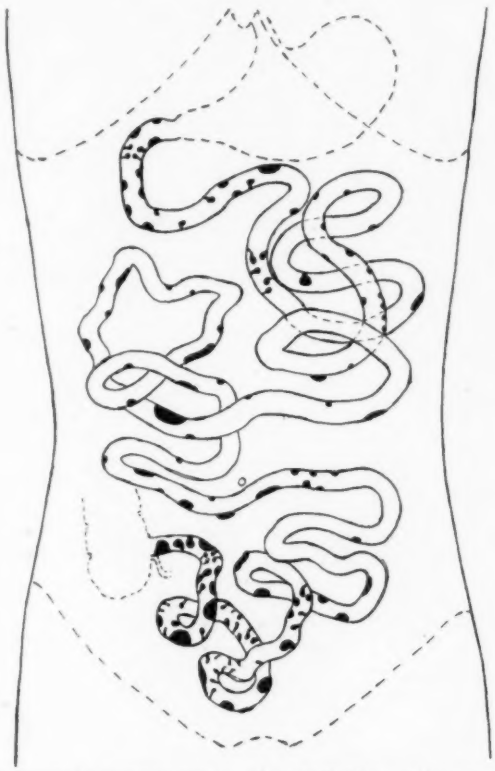


Fig. 1.—Diagrammatic representation of distribution of benign tumors throughout the small intestine. Note the smaller size, the predominance of the polypoid form and the greater frequency of localization in the lower ileum as compared with the malignant tumors in figure 2.

eighty-eight cases. The duodenum was most frequently involved, eight being located in that region, while the jejunum and ileum showed four and three, respectively. Adenomas were third in frequency, fifteen cases being found, eleven of which were located in the ileum. While these were the predominating types, attention should be called to the argentaffine group of tumors. Although these were formerly thought to occur only in the appendix, in this series seven were found in the small bowel,

five in the ileum and one in the duodenum. Lipomas, accessory pancreatic tissue and fibromas are among the other important benign tumors.

The distribution of the tumors throughout the small intestine is shown graphically in the accompanying diagrams. Figure 1 represents benign tumors, and figure 2, malignant. These are purely diagrammatic sketches for the purpose of showing the approximate locations and of

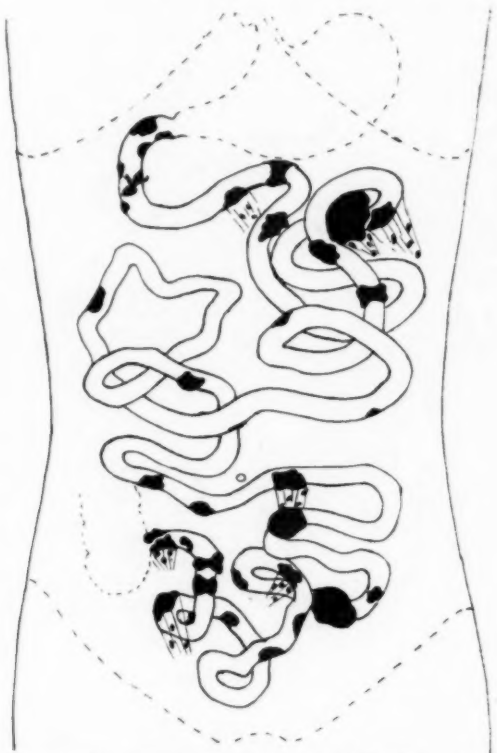


Fig. 2. — Diagrammatic representation of distribution of malignant tumors throughout the small intestine. Metastases are denoted by small dots in the lines radiating from the intestine. The tumors are larger and more invasive, and the points of election are the duodenum as well as the lower ileum. Compare with the distribution of benign tumors in figure 1.

contrasting the size of the gross tumors. Two features may be noticed at a glance. The terminal ileum is attacked much more frequently by both benign and malignant growths. The duodenum is next in susceptibility, whereas the jejunum is relatively free. The character of the growths is different in the two diagrams. Malignant tumors are larger, are usually single, and frequently show involvement of the glands or direct extension to the mesentery. Benign growths on the contrary, are smaller, often multiple and usually polypoid.

GENERAL TYPES OF TUMOR GROWTH

The type of growth assumed by neoplasms in the small intestine is worthy of note at this point, since a general classification holds for all tumors regardless of their histologic class or state of malignancy. The simplest classification deals with the direction that the tumor assumes

Fig. 3 (path. no. 16485).—Low power photomicrograph of the entire section through a lymphoblastoma of the ileum. This illustrates the polypoid type of tumor growth. The mucosa covered the base of the tumor and the pedicle, but was eroded from the surface.

in its growth, whether toward or away from the lumen of the intestine. Accordingly, they may be intralumenar or internal or, in contradistinction, extralumenar or external.

The external type (see fig. 14) is comparatively rare, occurring in only 5 per cent of this series. The determining factors are evidently two: the source of origin and the mechanical condition of free space. Growths originating in the outer layers of the intestinal wall find less resistance offered by the serosa than by the rest of the wall, unless the intestine at that point lies in proximity to an unyielding viscus. Malignant tumors with a predisposition to extension usually grow out into and along the mesentery and are consequently predominant among the external tumors.

The vast majority of intestinal tumors, especially the benign, assume the internal form, probably for reasons the converse of the foregoing. They commonly arise from the internal layers of the intestine where

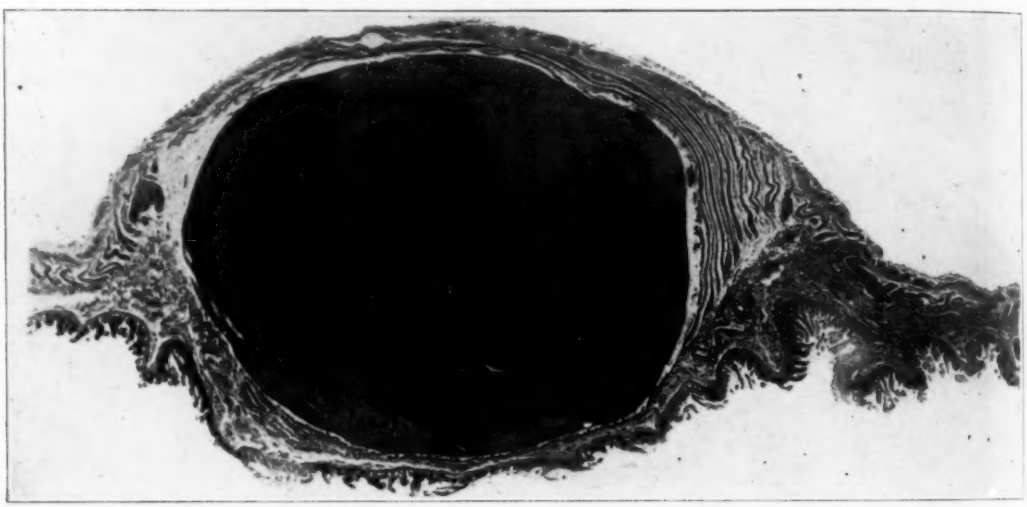


Fig. 4 (path. no. G10584, case 6).—Low power photomicrograph of the entire section through a myoma of the ileum. This illustrates the sessile type of tumor growth. The tumor arose from the circular layer of the muscularis. It was encapsulated and had pushed the normal submucosa and mucosa inward while forcing outward the longitudinal muscular layer and the serosa.

inward resistance is weakest. This type of tumor varies widely in form, but may be roughly classified as polypoid, sessile or extensive.

Polypoid tumors (fig. 3) are commonly benign, although it is not unusual to find in them secondary malignant change. They comprise the large group to which the diagnosis of intestinal polyp is often carelessly given. This term is loosely used by some pathologists as a final diagnosis, but while the majority are adenomas, almost any histologic type may assume the form of a polyp. They originate as small infoldings of mucosa into which the submucosa herniates, together with the tumor cells. The passing intestinal contents exert a constant force,

pulling and drawing on the base until a pedicle is formed, which may vary in thickness from a tiny thread to a thick cord 1 cm. or more in diameter, and in length from a few millimeters to 3 or 4 cm. This is the form of tumor that is often responsible for intussusception. Polyps rarely attain a size larger than that of a walnut before they are recognized by symptoms of obstruction. Multiple polyposis is not an infrequent occurrence.

Sessile tumors (fig. 4) are oval or round tumors of varying thickness. They may lie within the wall of the intestine and be classed as

Fig. 5 (path. no. 26163).—Gross specimen of a lymphoblastoma of the ileum. The lumen was almost completely blocked by a constricting growth. There was marked thickening and induration of the walls on either side of the constriction caused by infiltration of the tumor. Note the dilatation of the proximal and the collapse of the distal portions of the lumen. This represents the constriction type of tumor growth.

intramural, or they may be attached to the wall by a broad base. In either event, they are usually covered loosely by mucous membrane. Undoubtedly, they may become polypoid under the influence of the conditions described in the preceding paragraph. This form is usually assumed by benign tumors, but malignant tumors may be sessile before the process of invasion has extended to the surrounding tissues. The mucous membrane is intact, unless it is eroded by constant pressure of intestinal contents.

Infiltrative growth is used to designate the tumors, usually malignant, that originate in the wall and extend rapidly either around the lumen or in a longitudinal direction. They produce a jagged, irregular thickening, spreading out from the site of origin, blasting away the normal structure and eroding the mucous membrane.

The constricting type of tumor (fig. 5) is a variant of the preceding form, but is so definite and frequent as to deserve separate consideration. It is the result of a malignant infiltrating growth that encircles the lumen of the intestine, producing a constriction that in some instances is so great that a tiny distorted tubule is all that remains of the former lumen. This form of growth occurs with surprising frequency in the lymphoblastomas and may prove of some value in predicting the state of malignancy in this obscure group. Some of these tumors show a striking tendency to necrosis and excavation, so that the tumor remains a hollow irregular sphere through which the lumen passes, constricted at its points of entrance and exit. The center may become necrotic, and is often diagnosed as an abscess at operation and its true nature revealed only by frozen section.

PATHOLOGIC DATA

The pathologic study of this group of tumors is facilitated by dividing them into groups according to their malignancy. The malignant tumors include carcinomas and sarcomas. Lymphoblastomas constitute a borderline group and are considered separately. The remainder fall into the benign class and are composed of adenomas, fibromas, myomas, lipomas, argentaffin or carcinoid tumors, accessory pancreatic rests and angiomas. Enterocysts, cystic pneumatosis and neuroblastomas comprise a rare group of little clinical significance. Further subdivision of these groups will be made in order.

MALIGNANT TUMORS

CARCINOMAS

The literature on carcinomas is the most abundant, and many figures have been quoted regarding the relative occurrence. This is due not to the prevalence of this tumor so much as to the greater interest it has aroused. The incidence quoted by various writers varies somewhat, but it is generally agreed that carcinomas of the small intestine compose between 3 and 10 per cent of all gastro-intestinal carcinomas. This value was found to be 4.9 per cent in this series. Analysis of the 11,500 autopsy specimens from the general pathologic department yielded six cases, or 0.05 per cent. Carcinomas comprised 18.1 per cent of the eighty-eight tumors of this series.

Persons of "cancer age," or those in the fifth and sixth decades of life, are most susceptible to carcinoma of the small intestine. The

average age in sixteen cases was found to be 52. The oldest patient was 68 and the youngest 33 years. The male sex is most susceptible, being affected in eleven instances. No reason is known for the difference in incidence in men and women, but it agrees with the figures for carcinomas elsewhere in the intestinal tract. The disease occurs twice as often in the white race as in the colored. This variation, however, is coincident roughly with the ratio of the two races coming under hospital observation.

Fig. 6 (path. no. 26196, case 1).—Photograph of the gross specimen of an annular carcinoma of the jejunum. The tumor had produced almost total obstruction of the lumen, with proximal dilatation and distal collapse of the intestine. Note the persistence of the valvulae conniventes after dilatation.

Carcinoma is found more frequently in the duodenum than in any other portion of the small intestine in spite of its abbreviated length. This predominance is sufficient, even in this limited number of cases, to justify the conclusion beyond that of an accidental finding. Johnson disagreed, stating that if the papilla of Vater is excluded, carcinoma of the duodenum is almost unheard of. Clark agreed that the duo-

denum is most frequently attacked, and Vickers stated that carcinoma occurs in that location as often as in the rest of the small intestines combined. Although not borne out in this series of cases, the next susceptible site is commonly regarded to be the terminal ileum, while the remainder of the ileum and jejunum are infrequently the seat of malignant growth. Further subdivision of the duodenum is necessary to demonstrate the distribution of carcinomas. It is generally conceded that the second or periampullary region is most frequently invaded, and such was the case in seven tumors of this group. Three were located in the middle third, two of which involved the ampulla, two involved the first third, and two the terminal third.

Metastasis to other organs is the criterion *par excellence* for the estimation of malignancy and was found in four, or 25 per cent, of the

Fig. 7 (path. no. 44556).—Photograph of the gross specimen of an adenocarcinoma of the duodenum removed at autopsy. The tumor occupied one side of the intestinal wall and the edges were raised and curled over the ragged, ulcerated base. The lumen was blocked by encroachment of the tumor, and the patient died of intestinal obstruction. (Material obtained through courtesy of the Baltimore City Hospital).

cases. This is not as high as the incidence given by Craig or Clark, nor as frequent as metastasis from carcinoma of the stomach. The latter fact is explained by the earlier recognition of the condition in the small intestine. The first site of metastasis is the mesenteric glands. The next in order are the peritoneum, the liver and the lungs, but extension beyond the mesenteric lymph glands is rare.

The gross forms assumed by carcinomas of the small intestine may be grouped roughly in order of their frequency as follows: The constricting or stenosing form (fig. 6), the infiltrating ulcerative type (fig. 7) and the polypoid form (fig. 13). The size is exceedingly

variable. The smallest in this series were tiny submucous nodules a few millimeters in diameter, which appeared benign until the histologic sections were examined. The largest was the size of a grapefruit, infiltrating, ramifying and involving the surrounding structures. Those of the external type are rare, but attain the largest size in view of the fact that they do not cause early symptoms. The polypoid tumors rarely grow larger than a hen's egg before symptoms of obstruction reveal the presence of a pathologic condition. The color is pearly white, and the consistency is firm and hard. The mucous membrane may be intact over the early growth, but in the older infiltrative form, the mucosa is usually eroded, and a ragged ulcerated area designates the inner surface of the tumor. The tumor cuts almost like cartilage, is bluish white and looks fibrous.

Four main types of carcinoma occur in the gastro-intestinal tract: adenocarcinoma, medullary, scirrhous and colloid, as differentiated by their histologic characteristics. The first is by far the most common, the second much less frequent, and the last two very rare.

The term adenocarcinoma is used to designate tumors the cells of which have a tendency to retain their original glandular formation. They arise from the epithelial cells of the mucous membrane and grow rapidly into the wall of the intestine in sheets and strands, displacing the normal structural elements and forming typical glandular nests of cells. This glandular formation is so perfect, in fact, that the tumor could easily be mistaken for a benign glandular hypertrophy were it not for the cellular mitoses and extensive invasion characteristic of malignant tumors. The cells are commonly of the tall columnar variety, but may be cuboidal or even stratified. There is a moderate amount of pink-staining cytoplasm, at the base or middle of which lies the large, oval, hyperchromatic nucleus. Mitotic figures are abundant. While the cells remain in a more or less orderly arrangement about the acinus, these cell groups are scattered through the underlying tissue with utter disregard for the normal cellular structure, leaving the harassed fibrous and muscular tissue as a weakly ineffective supporting stroma. The mucosa covering the tumor is often the seat of erosion and secondary infection. One finds a sudden break in the normal mucous membrane under which the tissue is partially degenerated and harbors a dense cellular infiltration.

Adenocarcinomas do not always retain the pure glandular form described. The new cells apparently have little regard for the parent growth, and, after beginning the march of invasion, form sheets and nests of cells that bear only a rough resemblance to true acinar formation. The cells are round, irregular or cuboid, and are packed closely together. The cytoplasm is moderate in amount, and the nuclei are vesicular, vary in size and staining reaction and usually show mitosis.

Fig. 8 (path. no. 26196, case 1).—Low power photomicrograph of an adenocarcinoma of the jejunum. The tumor cells can be seen arising from the depths of the crypts and extending into and through the submucosa and muscularis. The alveolar arrangement of the cells is roughly preserved.

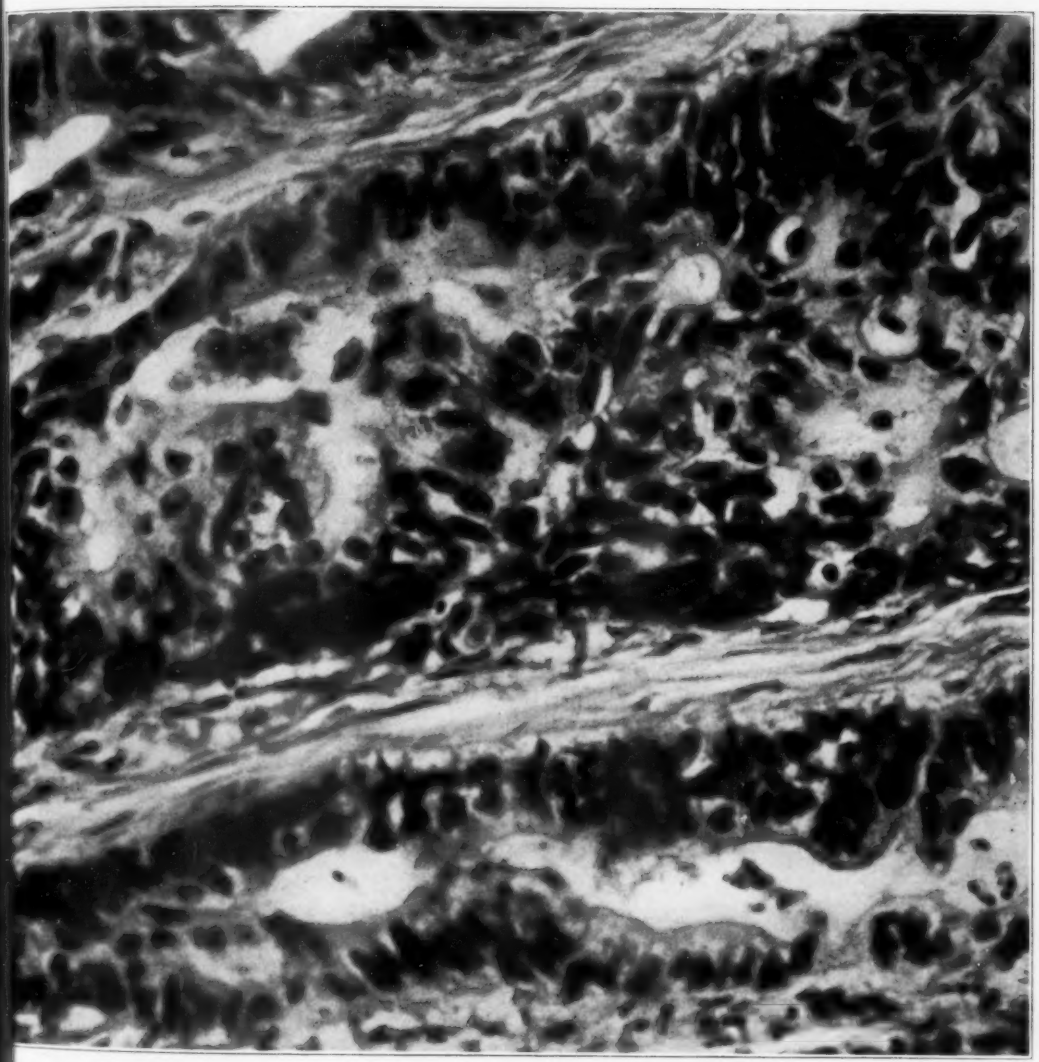


Fig. 9 (path. no. 26196, case 1).—Higher magnification of the tumor shown in figure 8. The photograph was taken through the lower part of the crypts. Note the atypical arrangement of the cells. The columnar shape has disappeared, and the cells lining the crypts are several layers deep. Some of the nuclei show mitoses.

The medullary type of carcinoma is softer and more spongy than the preceding type. It forms a fungating mass which bleeds easily. The cells are derived from the epithelial cells of the mucosa, but show no tendency to reproduce the glandular formation. This type of tumor

Fig. 10 (path. no. 26196, case 1).—Low power photomicrograph of a section taken from a lymph node in the vicinity of the tumor shown in figures 6, 8 and 9. The metastatic cells retained the property of alveolar formation. The steps of the reproduction can be followed in the upper right corner of the photograph. The individual cells are usually in a single layer, but are irregular in size. The columnar shape has been entirely lost.

is very malignant and spreads from the site of origin, recognizing no impediment to its progress. The cells form solid sheets and strands. They are closely packed, bearing a slight resemblance to squamous cell carcinoma. The cytoplasm is scant and takes a light eosin stain.

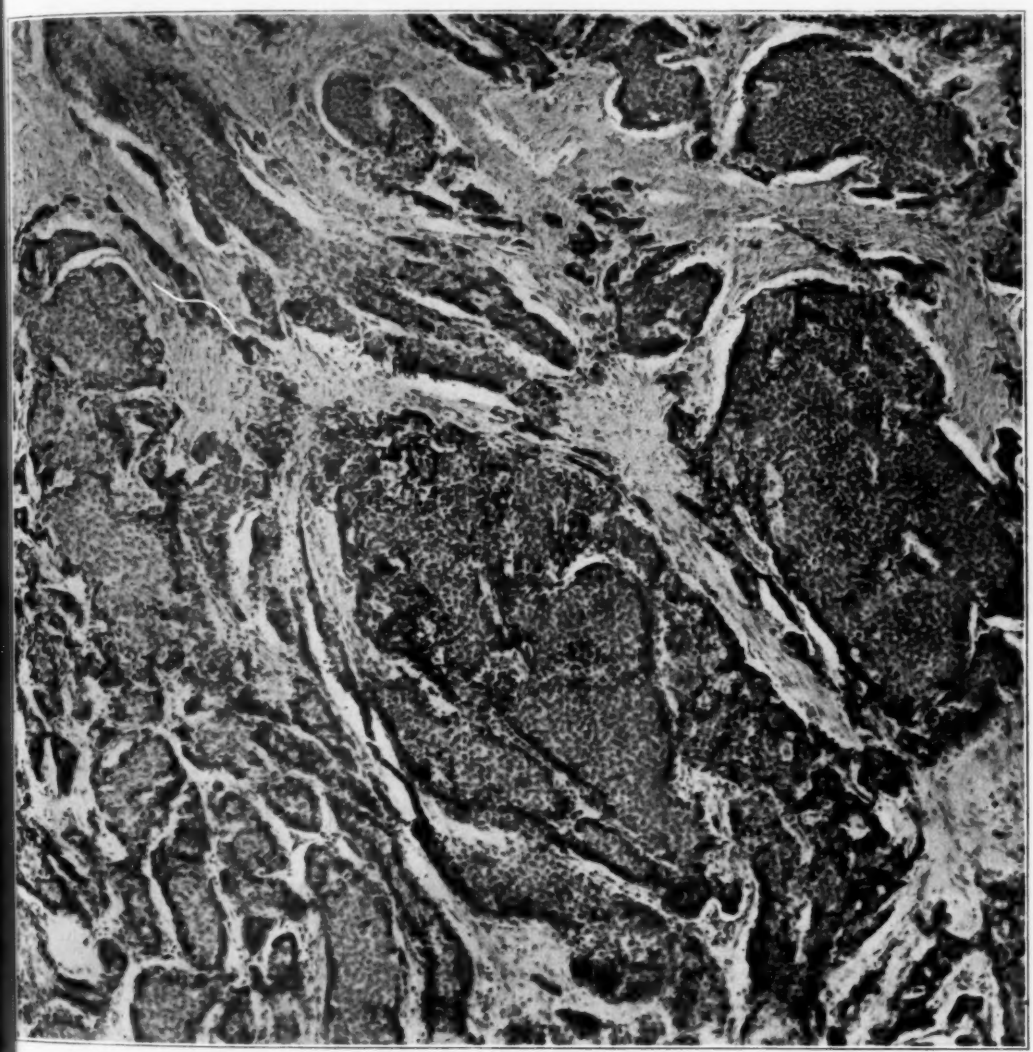


Fig. 11 (path. no. 31805).—Low power photomicrograph of a medullary carcinoma of the jejunum, metastasizing to the aortic glands. The cells are seen in solid strands and sheets invading the entire intestinal wall. Higher magnification showed a marked similarity between these cells and those of a squamous cell carcinoma. The cytoplasm is abundant, and mitoses are common.

The nucleus is large and light-staining, but contains numerous hyperchromatic particles. The submucosa and muscularis have either retracted before the advancing tumor edge or have been caught between the sheets of cells and compressed to narrow bands. Metastasis to glands takes place early, and the same situation is found. All of the normal glandular structure has either been replaced or pushed aside to make room for the metastatic cells.

Colloid carcinoma is very rare in the small intestine, but when it does occur, it assumes a form almost similar to the same type of tumor in the stomach, where it is not an infrequent invader. The tumor is largely external and consists of a lobulated gelatinous growth, fluctuant to the touch. The cut section shows a cystlike structure, the spaces of which are filled with a semisolid material that can be squeezed out. It represents a degenerate mucoid form of adenocarcinoma, according to Horsley.

It presents a characteristic histologic picture. According to MacCallum, two distinct types are found. The first is composed of cystlike cavities lined by a single layer of epithelium and filled with a glairy mucoid fluid. In the second type the cavities contain, besides the fluid, free tumor cells, each containing a drop of the same glairy fluid, which displaces the nucleus to one side and causes it to resemble the signet ring cell of Krompecher.

The pathogenesis of carcinomas in the small intestine is no less obscure than that of tumors elsewhere in the body. Certain facts have become established regarding their origin and manner of growth that may be considered authentic. Dewis and Morse stated that the intestine offers three possible points of origin. The epithelial cells of the mucous membrane give rise to the most common type, adenocarcinoma. A different type of glandular growth, which is less malignant, has been found to arise from the glands of Brunner in the duodenum. Aberrant pancreatic rests have been considered as a third source, but, since they are relatively rare, malignant change in them is of little importance.

The question of a malignant condition arising in a preexisting ulcer is still a mooted one. Although pathologists at large have not accepted this theory, the argument of MacCarty is convincing. Cases were found in this series that showed malignancy in the presence of an ulcer, but proof of the relationship is lacking.

Malignant change in an adenomatous intestinal polyp has received much consideration during recent years. Bordenhauer, Quinn and Landel first described the appearance of small areas of malignancy in an apparently benign adenoma. Subsequent treatises have supported the theory, until such malignant change is now recognized as a significant step in the histopathology of intestinal carcinomas. Tuttle claimed to have found evidence of malignancy in 75 per cent of his cases, while

Lockhart and Meisnery went so far as to predict ultimate malignant degeneration in all adenomas. Such a statement lacks supporting evidence and cannot be accepted at the present time. The presence of

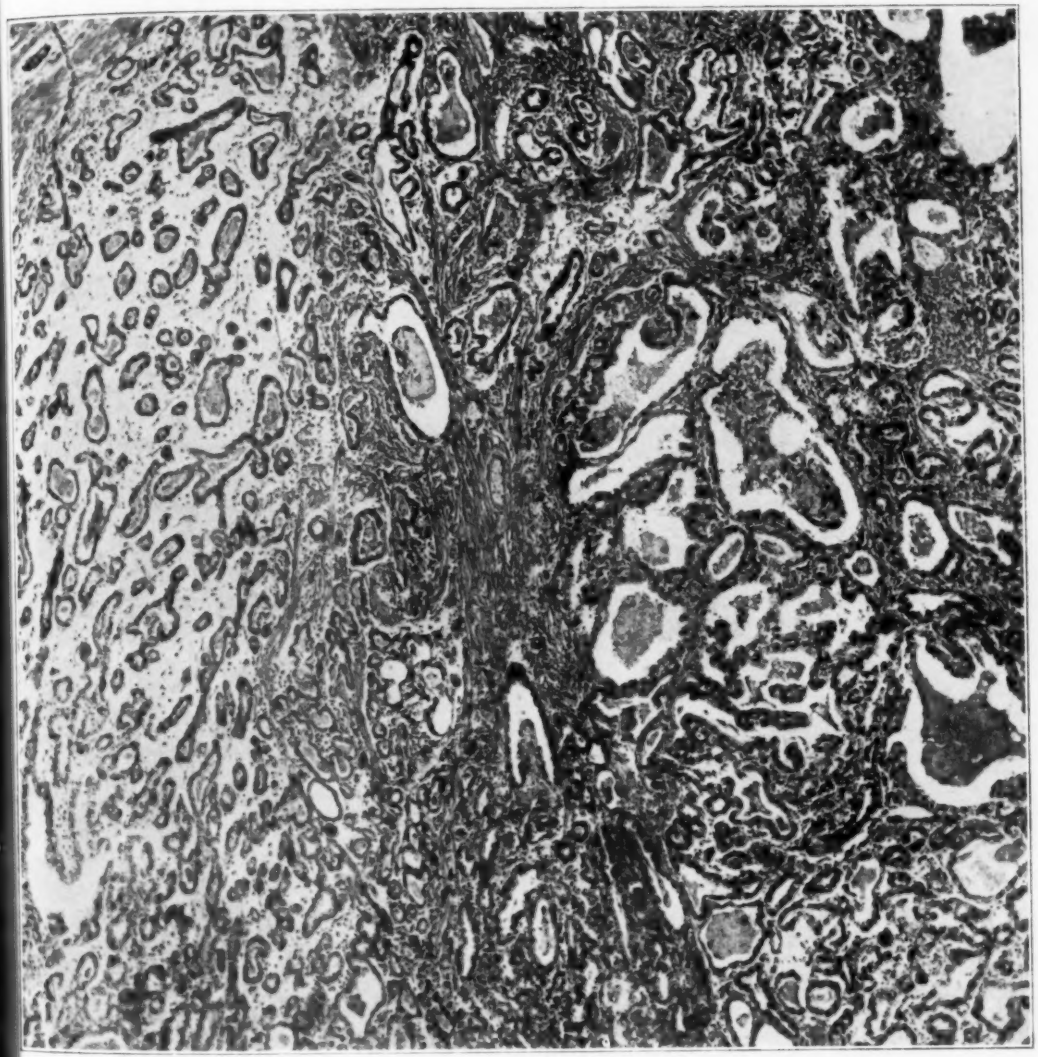


Fig. 12 (path. no. 46597).—Low power magnification of a papilloma of the duodenum undergoing malignant change. The cells composing the glands in the left and lower parts of the photograph are benign. In the right center, the glands are becoming dilated, and the cells are larger and more irregular. Mitotic figures were revealed by higher magnification (case of Dr. J. M. T. Finney).

malignant looking cells in an area of adenomatous hypertrophy is not sufficient to support the diagnosis of a malignant condition. At least

two conditions must be fulfilled; there must be definitely cancer cells, large, irregular and with mitoses, together with invasion of the basement membrane. The presence of metastases in advanced cases of course makes the diagnosis certain. Malignant degeneration is not, as the name implies, a degenerative process in which preexisting normal cells are converted into cancer cells. Carcinoma cells are self-propagative, and, once they have become established, an entirely new tumor growth follows. The adenoma may be considered as hypertrophied normal mucosa which is subject to invasion by carcinoma, just as the normal epithelial lining is, but which, through an abnormal arrangement, has been made more susceptible. Consequently, the typical picture of this condition is that of a benign polyp toward the edges of which areas of typical adenocarcinoma have arisen. These may have

Fig. 13 (path. no. 46597).—Gross specimen of the tumor shown in figure 12. The tumor arose from the duodenal wall just distal to the pylorus, and formed a fungating mass projecting into the lumen. Partial gastrectomy was performed, but the patient died of secondary infection of the abdominal wound and septicemia (case of Dr. J. M. T. Finney).

grown inward, pushing aside the benign portion of the polyp, but they more commonly grow outward as fungating masses of tumor. Such a tumor, showing malignant change, is shown in figures 12 and 13.

The mechanism of glandular reproduction in the growth of adenocarcinoma is an interesting pathogenic feature. This seems to be an inherent tendency of the mucosal cells. The youngest cells of the growth, found at the advancing edge of the tumor, do not show a glandular arrangement. This is also demonstrated in metastases to glands. The earliest invading cells are grouped in solid strands and nests. As growth progresses, they tend to arrange themselves in a circular fashion. The nuclei then retreat to the part of the cell farthest

from the center; vacuolation appears in the dentral ends of the cytoplasm, and finally this gives way, forming a hollow ring. These cells at no time show the typical columnar shape found in the parent epithelium. This process is admirably illustrated in figure 10.

The prognosis in cases of carcinoma is far from encouraging. If metastases have occurred, the ultimate result is uniformly fatal, and little can be done for the patient except the institution of palliative treatment. Fourteen of the sixteen patients in this series are known to be dead, and follow-up reports on the remaining two were unavailable. Even in the cases without apparent metastases, the patient usually succumbs to a recurrence of the tumor after removal.

SARCOMAS

The small intestine is the seat of tumors of mesoblastic origin in rare instances. The types commonly found are pure or variant forms of fibrous or spindle cell sarcoma, and are roughly the same as those found to occur in the stomach and large intestine. Among the miscellaneous types are included mixed forms, such as myxosarcoma and myosarcoma. The large group known as the lymphoid group of tumors may or may not be true sarcoma. They have been the subject of much discussion, and since their true nature is still obscure they are considered separately as a borderline group.

True sarcoma is rare in the small intestine as well as in the rest of the gastro-intestinal tract. Telling reported a spindle cell sarcoma in a child of 3 years, and Libman reported, in 1900, a case of similar nature in a white man of 42 years. Two cases are reported in this series, one of the spindle cell variety and the other a myosarcoma. Both patients were in the fifth decade of life. It is impossible to draw conclusions as to sex and race preferences in so small a number of cases.

The ileum is the site of election for sarcoma. Although one of the two cases was located in the jejunum, the other, with those reported in the literature, arose in the ileum. These sarcomas do not metastasize as readily as carcinomas. When metastasis does occur, the mesenteric glands are most frequently involved first, after which secondary invasion may reach the liver or lungs.

Sarcomas tend to assume the external type, growing out into the mesentery rather than into the lumen (fig. 14). The gross form is usually rounded, lobulated and encapsulated, in contrast to the finger-like ramifications found in the advancing border of a carcinoma. Early tumors are usually hard and elastic. In the more advanced stages they may have a soft spongy feeling, if central necrosis has occurred. The cut section is white and translucent. The size is variable, but often attains that of a child's head. One of the tumors in a case reported

in this series was as large as a grapefruit, around which the lumen of the jejunum stretched as a flattened tube.

Low power microscopic examination of a fibrosarcoma reveals the tumor to be composed of whorls and solid strands of connective tissue cells. Higher magnification shows typical spindle-shaped cells of fibrous connective tissue. They have a moderate amount of light-staining cytoplasm, in the center of which is located an elongated nucleus which also stains lightly, but shows numerous chromatin particles. These

Fig. 14 (path. no. 44558, case 2).—Gross specimen of a large spindle cell sarcoma of the upper jejunum. The flattened lumen of the intestine can be seen encircling the lower part of the tumor. Note the central necrosis. The tumor arose from the jejunal wall and grew outward into the mesentery. Metastases had occurred in the liver. When first seen, the condition was judged inoperable, and the patient was treated palliatively. Specimen removed at autopsy (material obtained through the courtesy of Dr. MacCallum).

cells may be mistaken for round cells in some part of the section but this is due to the fact that the cells are here cut in coronal section. Fibroblasts are not infrequent, and are found in great abundance near the younger part of the tumor at the advancing edge. The most inter-

esting feature of sarcoma in general and one of the best criteria of malignant change is the total disregard that the cells seem to hold for the vascular system. They invade the smaller capillaries and arterioles, and in many instances may be found to occupy the lumen of the vessel.

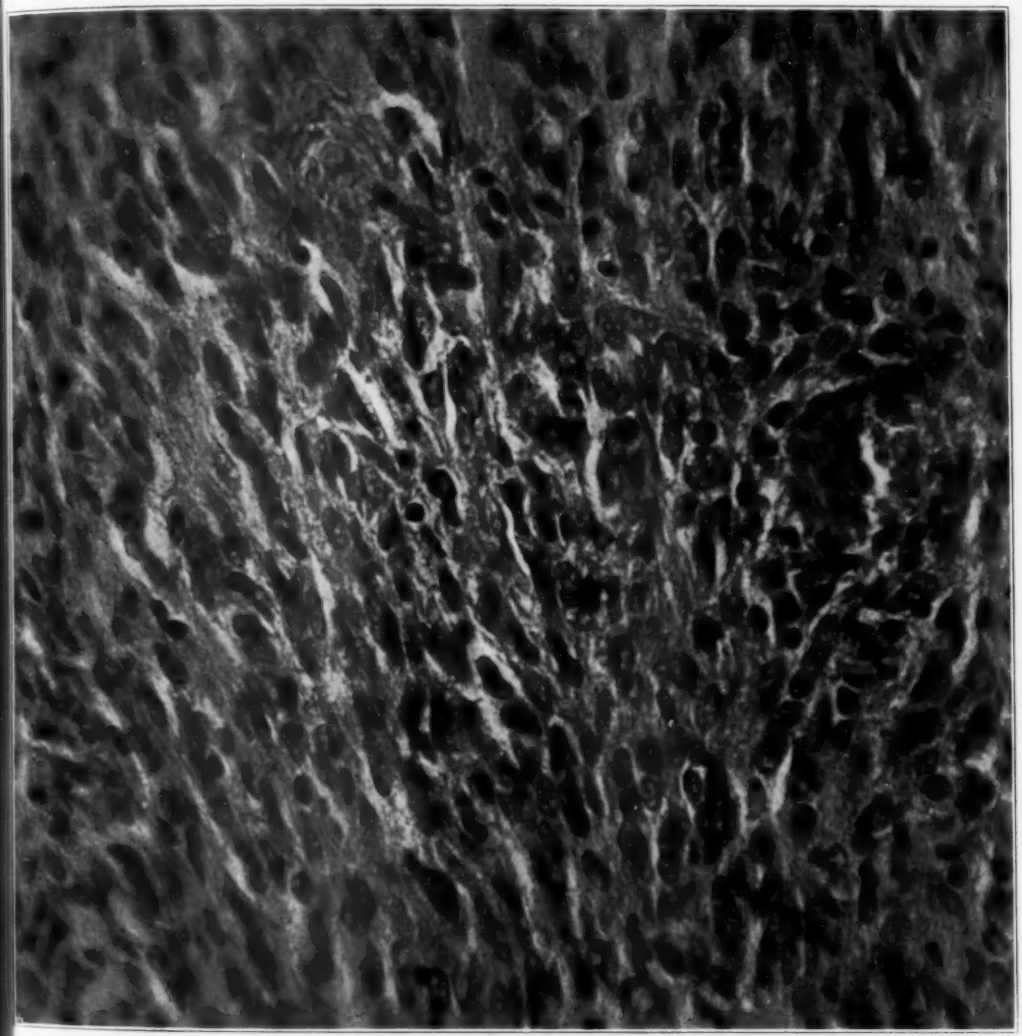


Fig. 15 (path. no. 44558, case 2).—High power photomicrograph of the tumor shown in figure 14. The cells are long and spindle-shaped and contain a large oval nucleus, in which mitotic figures can be seen. Note the beginning invasion of the capillary wall by tumor cells. Occasional fibroblasts can be seen.

A moderate cellular infiltration is present in almost every case. This consists of cells of the lymphocytic and myelocytic series and is greatest

when secondary infection has taken place. Vascularity is more marked than in carcinomas, and numerous capillaries can be seen throughout the tumor.

Myosarcoma presents an almost identical picture and is often confused with the spindle cell variety of fibrosarcoma. The cells arise from muscle tissue, however, and, although atypical, they retain certain characteristics that serve to distinguish them. The cytoplasm stains brighter pink with eosin, is thicker and more plump than that of fibrosarcoma. The nucleus is larger, hyperchromatic and shows many mitotic figures. One gains the impression, in fact, that the nuclei compose the essential part of the picture, and that the cytoplasm is crowded in as a supporting stroma. The tumor growth can usually be traced to an origin in the muscular coats of the intestinal wall. This type of sarcoma is not as vascular as the spindle cell variety, but shows the same tendency toward invasion of the blood vessels.

Myxosarcoma is popularly considered to be a degenerate form of spindle cell sarcoma and should not be confused with the pure form of myxoma found in other organs and thought to be of neurogenic origin. One finds, on examination, light areas scattered between strands of spindle cells. These areas show a faintly granular basophilic cytoplasm divided by isolated spindle and star-shaped cells. The matrix of these cells varies greatly in amount, but is apt to be grouped around blood and lymph vessels. Vascularity is marked, and the capillaries stand out prominently in the myxomatous area.

The pathogenesis of this group of tumors is fairly clear, but little can be said regarding the etiology. Sarcomas arise as abnormal proliferations of cells from any tissue of mesenchymal origin. These tissues in the small intestine are the connective tissue of the submucosa and subserosa and the smooth muscle tissue of the muscularis; hence the two types, fibrosarcoma and myosarcoma. Myxosarcoma, as just described, does not constitute a separate pathologic entity. The name is purely descriptive and is often used in the combined form.

Very little can be said regarding the etiology of these types of sarcoma. Nothnagel has suggested a chronic infectious process as being contributory. His discussion, however, included the lymphoblastomas, and probably does not apply to the pure types of sarcoma.

Sarcomas of these types give a better prognosis than carcinomas, for the reason that metastasis occurs less freely. The tumors grow more slowly and do not tend to break away from the circumscribed form early in growth. When recognized early and excised, the tumor does not tend to recur, and the patient may recover entirely.

LYMPHOBLASTOMAS

There is no group of neoplasms about which more confusion of nomenclature and classification exists than the lymphoid tumors of

the small intestine. They have been discussed in the literature under a variety of names, a few of which are lymphosarcoma, round cell sarcoma, lymphocytoma, chronic inflammatory tumors, Hodgkin's disease, pseudoleukemic granuloma, lymphoid granuloma and many others.

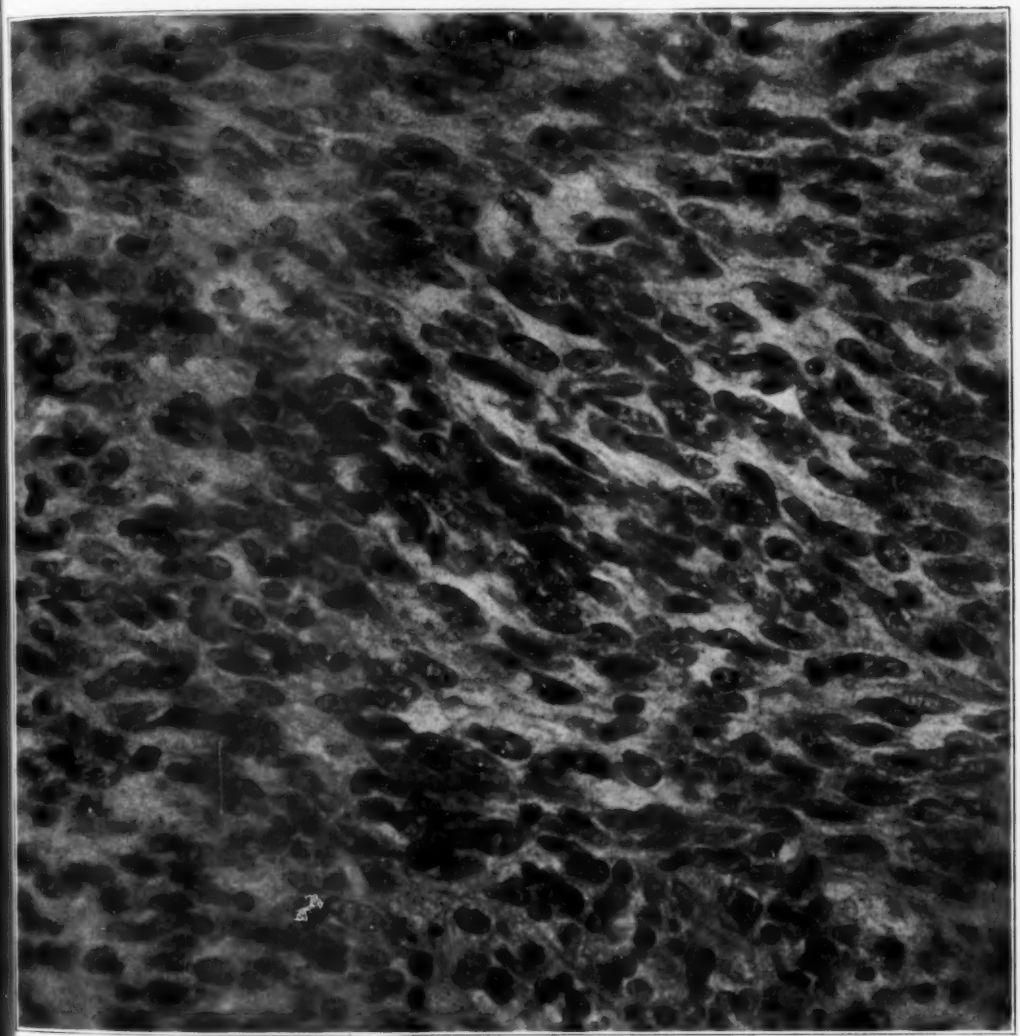


Fig. 16 (path. no. 37600).—High power photomicrograph of a myosarcoma of the ileum. The tumor caused no symptoms, but was found accidentally during operation for a ruptured appendix. The cells are large, contain a moderate amount of cytoplasm and large, plump, elongated nuclei with abundant mitoses. The origin of the tumor could be traced to the circular layer of the muscularis.

They have undoubtedly been known and recognized under some of these terms for many years. Baltzer, in 1873, noted their frequency in the

small bowel and reviewed a number of cases, classing them as sarcomas. Libman reported four cases in 1900 as lymphosarcomas. Crowther gathered 122 cases from the literature in 1913, and again in 1919 Graves extended the list to include 249. The latter noted the confusion surrounding a suitable classification and asked that all such tumors be included under the general term of lymphoblastoma. Körte added two cases of his own in 1921, making the assertion that tumors of this type show characteristics of neither a true malignant tumor nor a specific process. He therefore suggested that they be classed as tumors of a nonspecific chronic inflammatory process. Liu, working in this clinic, added nine cases in 1925, frankly admitting his inability to distinguish malignant from nonmalignant forms. The term "chronic inflammatory tumor" has long been used in this hospital, but it is a poorly descriptive term, since it leads one to suspect neither the true tumor formation nor its origin and manner of growth. After consideration of all aspects of the question, Graves' term of lymphoblastoma has been accepted in this article as being the most descriptive, with certain modifications. Lymphoblastoma, according to Mallory's definition means "a tumor of mesenchymal origin of which the cells tend to differentiate into cells of the lymphocytic series." Further differentiation depends largely on the degree of malignant change exhibited by the tumor cells, and will be discussed more fully in a subsequent paragraph.

The small intestine seems peculiarly susceptible to this type of tumor. Twenty-one of the eighty-eight tumors of this series were diagnosed lymphoblastoma. They occur about twice as frequently in the small intestine as in the large. Comer and Fairbanks stated that 63 per cent of gastro-intestinal lymphoid tumors occur in the small bowel. Staemmler, classing such tumors as lymphosarcomas, placed the incidence at 62 per cent. It is sufficient to say that lymphoblastomas of the small intestine are by no means a rare occurrence, as is shown by Graves' collection of 249 cases from the literature.

This tumor may attack persons of any age, although statistics show that it occurs in young persons with far greater frequency than do other malignant tumors. The average age of patients included in this series was 32, the youngest being 5 and the oldest, 77 years. Distributed according to decades of life, this group was approximately equally divided between the first five.

White males show an apparent susceptibility to this tumor. Sixteen were affected as compared with five females, and eighteen of the patients were white as compared with three colored. This variation is greater than one can ascribe to chance, although it is impossible to account for it.

Lymphoblastomas show a striking predilection for the terminal ileum. All of the twenty-one cases here reported, with the exception

of one, were located in the terminal 100 cm. of the ileum, this one exception occurring in the middle third of the duodenum opposite the papilla of Vater. Several other instances were found in which the tumor involved the terminal ileum and the cecum together, but since it was impossible to determine the point of origin, they have not been included in this series.

Tumors of the lymphoid series do not metastasize as readily as either true sarcomas or carcinomas. The absence of this feature undoubtedly jeopardizes the estimation of their state of malignancy, and this has given rise to the chief difficulty in diagnosis. When metastases do occur, the adjacent mesenteric lymph nodes bear the brunt of the attack, but extension beyond them does not follow any set course. One patient showed a recurrence of the original tumor in the abdominal wall following operation. Another was operated on for a tumor of the brain, which was found at autopsy to be secondary to

TABLE 4.—*Distribution of Lymphoblastomas According to Age*

Age	Number of Tumors
1 to 10 years	3
11 to 20 years	4
21 to 30 years	2
31 to 40 years	4
41 to 50 years	4
51 to 60 years	2
61 to 70 years	1
71 years and over	1
Total	21

lymphoblastomas in the ileum. Kundrat attempted to explain metastasis from these tumors solely by way of the lymph channels. Ewing argued that in some instances secondary growths are found in locations that can be explained only on the basis of transportation by means of the blood stream. Such a view is supported by the second case just mentioned. In the face of such evidence it seems that one must assume that the malignant cells may be dispersed by either channel or by direct extension.

The gross pathology of lymphoblastomas is variable. Their size may vary from a small thickening of the wall in the region of the agminate nodules to that of a grapefruit, if the tumor is external in type. The most common form assumed by the tumor is that of a constricting growth encircling the lumen. This happens so frequently that it is almost characteristic of the tumor and supports the diagnosis of malignancy in cases of doubt. The growth begins on one side of the wall and extends around the lumen. Extension may also proceed in the longitudinal direction of the intestine followed by a dilatation in the center of the tumor, so that the final picture is that of a hollow sphere constricting the lumen at its points of entry and exit. Extension to the

mesentery may also take place, but this is not the rule. The majority of the tumors present smooth unbroken surfaces. Still another form sometimes found is that of multiple polyposis; these tumors resemble adenomas in their gross form, but they are microscopically lymphoid tumors. Such a condition might be designated as multiple lymphoblastomatosis.

The texture of the tumor, especially in the advancing edge is firm and fibrous, and the cut edge is bluish white. Central necrosis with excavation is not an unusual feature. Some of the latter type have been diagnosed abscesses when on incision of the wall a quantity of

Fig. 17 (path. no. 41291, case 3).—Gross specimen of a lymphoblastoma removed from the ileum at operation. The tumor resembles roughly a hollow sphere. The lumen was constricted at the points of entry and exit, while between the two there was a dilatation. The walls were thickened by invasion of the tumor. The mucosa was intact but hyperemic. The patient died three months later from recurrence (case of Dr. J. M. T. Finney).

purulent necrotic material escaped, and the malignant nature of the tumor was recognized only by frozen section.

The histologic picture is subject to the widest variation, although certain typical cellular elements are common to all types. Differentiation is based in general on the preponderance of these cells and is a modification of Ewing's classification. Thus there are four main groups: (*a*) nonspecific granulomas, (*b*) reticulum cell sarcoma, (*c*) malignant lymphocytomas and (*d*) endotheliomas.

Nonspecific Granulomas.—These tumors are most frequently found as inflammatory thickenings, polypoid growths or fungating masses in the lower ileum, but are rarely found in the constricting form. The overlying mucosa is seldom ulcerated, and the condition may pass unrecognized unless some form of obstruction occurs. With low power magnification the tissue is seen to consist of a cellular infiltration beginning in the loose connective tissue of the submucosa, and later invading the muscular coats, splitting apart the fibers but not destroying the normal architecture of the wall. The predominating cell is a small round cell which, with high power, resembles closely the lymphocyte of the blood stream. A small, light rim of cytoplasm surrounds the nucleus, which is also small and very dark-staining. Especially abundant are

Fig. 18 (path. no. 18427).—Gross specimen of a large pedunculated tumor arising in the lower ileum and causing an ileocecal intussusception. The cecum and terminal ileum were resected, and the patient made an uneventful recovery. The histologic diagnosis was lymphoblastoma (case of Dr. J. M. T. Finney).

plasma cells with a slightly larger nucleus and a larger amount of cytoplasm. Polymorphonuclear leukocytes appear in fewer numbers, and in some sections eosinophils are found. The stroma consists of normal strands of connective tissue and muscle fibers, somewhat distorted but not grossly invaded or destroyed.

The symptoms of tumor as a whole are similar in many respects to those of a specific infection, and diagnosis is often extremely difficult. The absence of positive clinical data characteristic of a specific infection, however, point toward the diagnosis of a tumor of lymphoid origin.

Reticulum Cell Sarcoma.—One of this group of tumors apparently takes its origin from the reticulum cells of the primordial follicles and

cords, the so-called reticulum cell sarcoma (figs. 19 and 21). The microscopic picture is characterized by a preponderance of reticulum cells scattered irregularly throughout the tumor. These are large cells

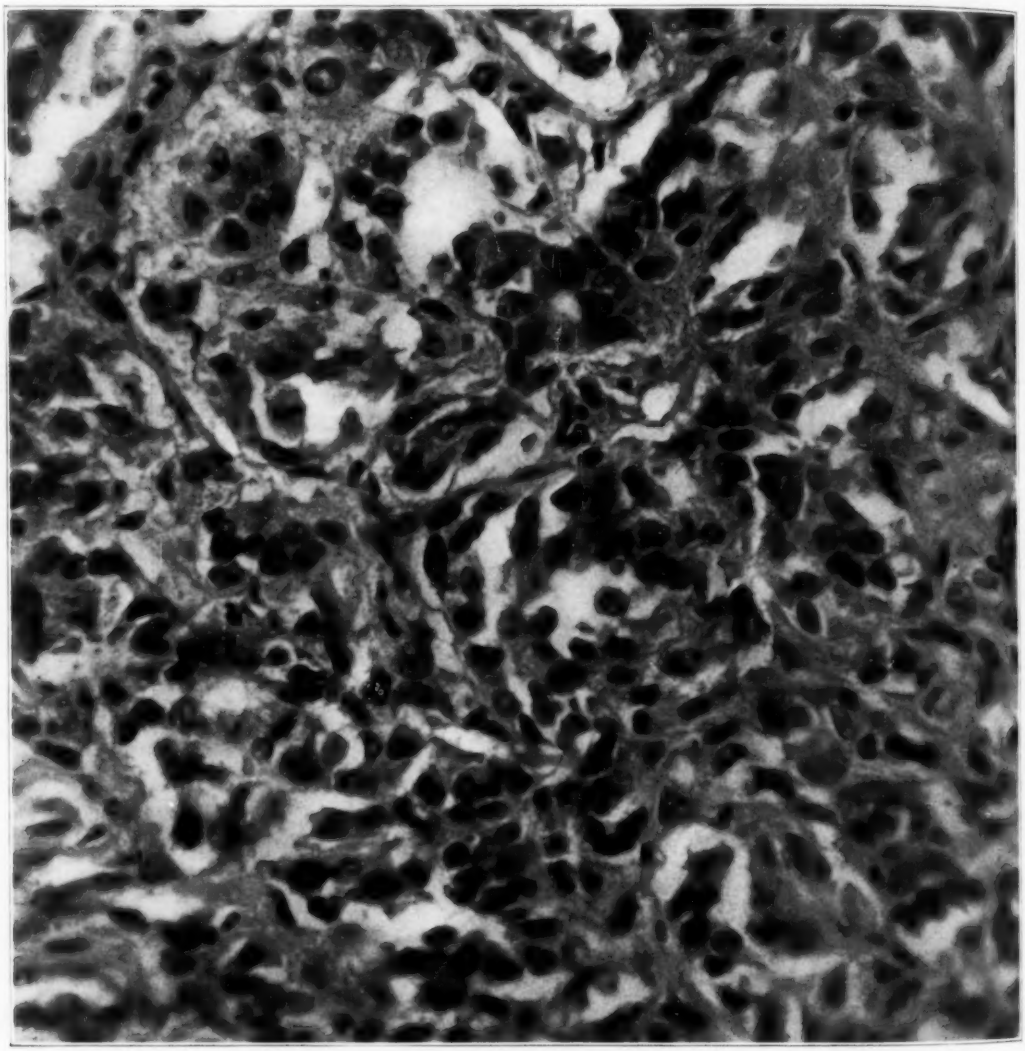


Fig. 19 (path. no. G6346).—High power photomicrograph of a lymphoblastoma of the ileum. The cells are polygonal and irregular in size, and there is an abundance of reticulum. Occasional large giant cells may be seen, and throughout the tumor is an admixture of small round cells. This is the reticulum cell type of sarcoma.

with a light-staining nucleus, which shows numerous mitotic figures. The cytoplasm is abundant, irregular and takes a bright pink stain with

eosin. The reticulum is variable in amount, being almost negligible in some areas, while in others it constitutes a profuse fibrous overgrowth. There is a scattering of small lymphocytes, leukocytes, eosinophils, plasma cells and occasional large giant cells. The latter possess a nucleus with a diameter at least twice that of the reticulum cells and a narrow rim of cytoplasm. They stain more darkly than the average lymphoid cells. Their nature is obscure, but it is assumed that they represent atypical cells of the lymphoid series. Vascularity is not marked but it is not unusual to find capillaries that have been invaded by tumor cells. Fragments of mucosa and normal tissue of the intestinal wall are found, especially near the edges of the tumor, but little of the normal structure is left. The tumor is clearly invasive rather than infiltrative.

Malignant Lymphocytoma (fig. 20).—This is the type most commonly found and is the form usually confused with lymphosarcoma. It represents a misdirected development of the normal lymphocyte. It appears apparently first in the agminated nodules, where it rapidly increases in size, compressing and forcing out the normal structures of the lymph node, after which it grows by extension, usually in the constricting form described elsewhere. The predominating cell type is one that resembles closely a large lymphocyte. The nucleus is much larger, however, and vesicular with many or few chromatin particles. The cytoplasm is scanty and takes a light stain. It is very difficult to distinguish this type of cell from a reticulum cell when the reticulum is lacking. Some of the cells are smaller, but are clearly cells of the same series. They represent intermediate forms between the lymphoblast and the mature tumor cells. These cells are closely packed together with little or no supporting stroma. They have the appearance of a younger cell near the advancing border of the tumor, with the smaller, darker staining nucleus of the intermediate form. The same admixture of leukocytes and plasma cells with occasional giant cells is common to this as well as to the preceding type. These are especially marked near the borders of the tumor. Vascularity is marked, and capillaries are scattered throughout. These are peculiarly susceptible to the invasion of the tumor cells, and in places the endothelial lining is broken through and the lumen filled with malignant looking cells. The large giant cells already described are not an essential part of the picture, but large multinuclear cells are not uncommon.

Endotheliomas.—One must consider the possibility of endotheliomas arising from the endothelial cells of the lymph nodes. These, if they occur at all, are so rare in the intestine that a discussion of their pathology is unwarranted.

The histogenesis of the lymphoblastomas as a group is still obscure, but in an attempt to clarify the situation, it is assumed that these tumors

arise from lymphoid tissue as atypical cell types, for two reasons: First, practically all of them are found in the terminal ileum, where the agminate nodes are known to occur with the greatest frequency. Furthermore, it is not uncommon to find a tumor developing directly

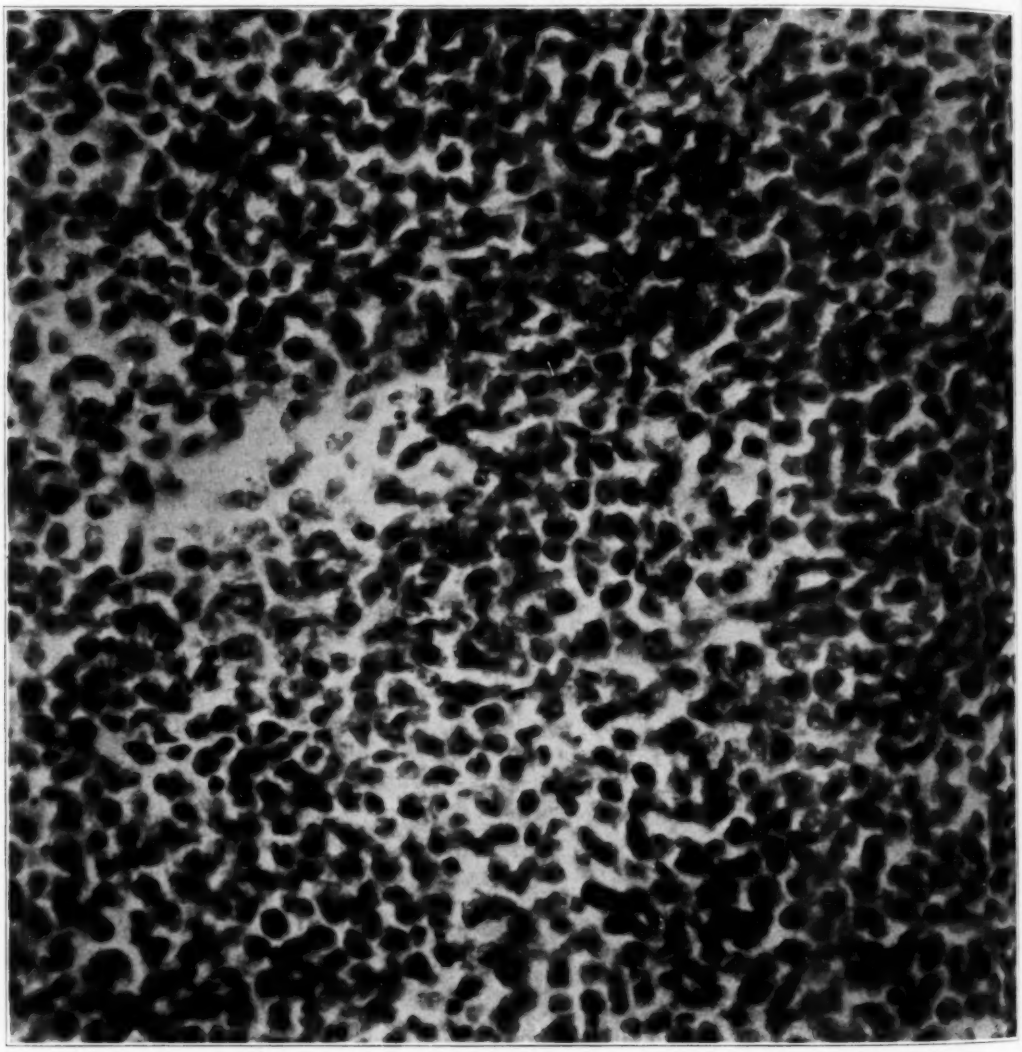


Fig. 20 (path. no. 16485, case 9).—High power photomicrograph of a lymphoblastoma of the malignant lymphocytoma type. The cells are densely packed together in a homogeneous mass. They are round but irregular in size. The cytoplasm is scanty, and the nuclei are large and hyperchromatic. Smaller cells resembling true lymphocytes are seen, and between the two types may be seen all stages of gradation. There is little or no reticulum or stroma (case of Dr. G. J. Winthrop).

from one of these nodes or patches as a proliferation of large atypical cells which disrupt the normal histology of the node and later penetrate the structures of the intestinal wall. In the second place, the cells comprising the tumor show plainly all gradations from that of a normal lymphocyte to the large, malignant tumor cell. What causes the lymphoblast to assume the malignant form is a different matter. Stasis

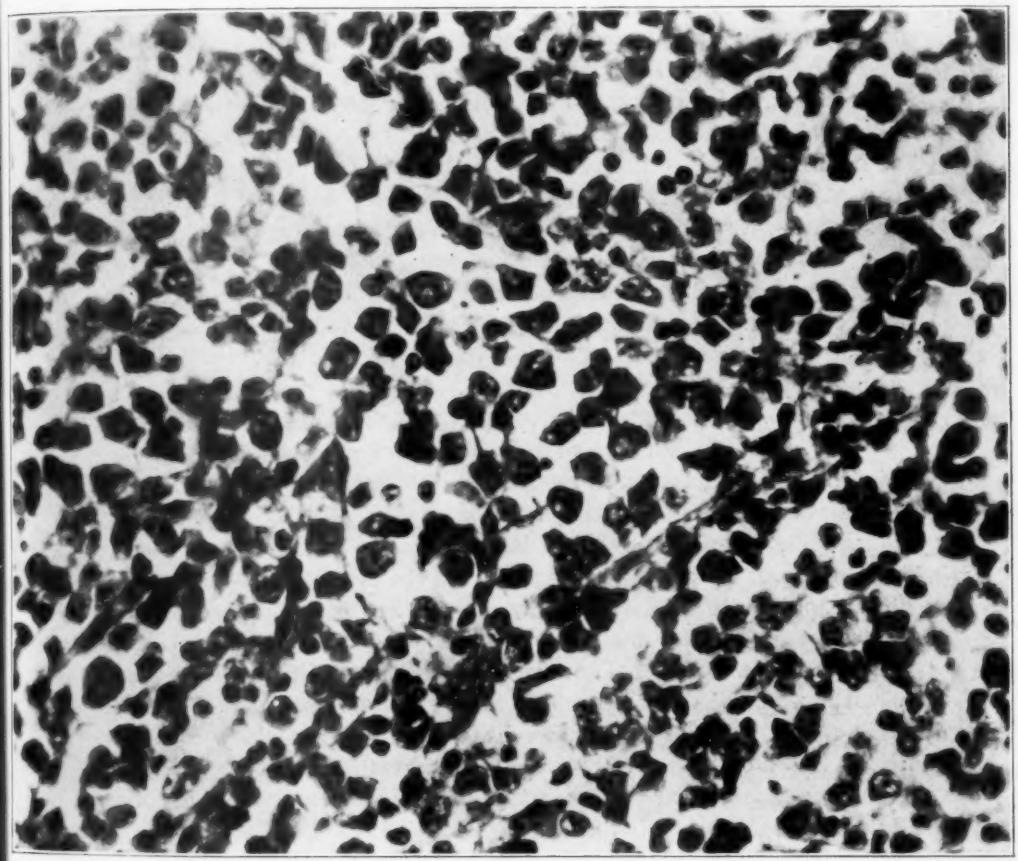


Fig. 21 (path. no. 41291, case 3).—High power photomicrograph of a lymphoblastoma. This is a reticulum cell sarcoma of a slightly different type from that shown in figure 19. The cells are large and polygonal, vary greatly in size, and are not so closely packed as in the preceding photomicrograph. The nuclei are large and vesicular, and the cytoplasm is moderate in amount. There is a moderate amount of reticulum scattered throughout the section. The tumor cells are invading a capillary in the upper portion of the picture.

and irritation, as discussed in a previous paragraph, may play a part, but this remains to be proved.

Assuming that the growth is of lymphoid origin, there remains the question of diagnosis, which is far more important. It concerns itself with two phases, that of classification and that of malignancy. For reasons previously stated this group of tumors is considered under the general heading of lymphoblastomas. Ewing, discussing the histogenesis of lymphoid tumors in general, classified them according to their three possible cellular prototypes as follows: 1. Lymphocytes may give rise to the benign group of lymphomas or granulomas or to the malignant lymphocytomas commonly known as lymphosarcomas. 2. Reticulum cells are the source of the reticulum cell sarcoma or large cell sarcomas. This is the tumor commonly referred to in the literature as round cell sarcoma and is practically always malignant. 3. Endothelial cells, may give rise to endotheliomas, although this type of tumor is rarely found in the intestine. It is possible to subdivide these groups further, but for practical purposes this is sufficient.

The second and by far the most important aspect of diagnosis is the determination of the state of malignancy of the tumor. The pathologist is accustomed to consider metastasis as the criterion of malignancy. Recurrence following the excision of a tumor is also indicative of malignancy. When this occurs the diagnosis is simple, but at this stage is not of prime importance, since the chances of curing the patient are very poor. It is a case of valuable "positive" and valueless "negative" information, for when metastasis has not occurred and the patient is presumably cured following excision, it is impossible to foretell the course of events had the patient been untreated. This cannot be relied on, therefore, for accurate diagnosis, and the best index of malignancy is the appearance of the cells themselves. Experience has shown that the reticulum cell sarcoma is the most malignant of this group. Nevertheless, since metastases do occur in instances in which the microscopic picture cannot be differentiated from that of tumors that remain localized, the lymphoblastomas must be considered potentially malignant until the clinical course has proved them otherwise.

The relation between certain infectious processes and the lymphoid tumors is interesting but confusing. That tuberculosis and syphilis sometimes simulate true tumors is well known. The cellular infiltration that they occasion is largely lymphocytic and the differentiation is very difficult in the absence of relevant clinical points. For obvious reasons specific infections have been omitted in this study since they form a discrete group in themselves.

Lymphoblastomas comprise a borderline group of tumors in regard to malignancy. Metastasis is not constant, and in cases in which it has not occurred the prognosis is good. Lymphoblastomas seldom recur following excision, but the surgical procedure should include

resection of a portion of the normal intestine on either side of the tumor. In any event, it is by far safest to consider the tumor as potentially malignant and to treat it as such.

BENIGN TUMORS

ADENOMAS

Adenoma is the type of benign tumor most commonly found in the small intestine. It seldom attains a size sufficient to cause obstructive symptoms, however, and the majority were recognized only at autopsy. Adenomas comprised fifteen of the eighty-eight tumors in this series, or 17 per cent. Herteaux placed this value at 14.3 per cent while King found it slightly higher, namely 19 per cent. Balfour and Henderson, considering only the benign tumors, found adenomas in 40 per cent of the cases. Saint, who has given the best review of the subject to date, put their incidence at 8 per cent of all tumors of the small intestine, but found them third in frequency among benign tumors.

The age limit is exceedingly variable. The youngest patient in this series was 6 months and the oldest 62 years of age, the average age being 33.5 years. Symptomatic adenomas tend to occur in younger people. No race and neither sex shows any particular susceptibility to this tumor.

Adenomas increase in frequency toward the lower part of the intestinal tract. In ten of the fifteen cases they were located in the ileum. King noticed this fact and commented on finding all of his five cases in the ileum. Golden reported eleven cases arising in the duodenum, however, five of which originated from the cells of Brunner's glands. All writers agree that adenomas of the jejunum are extremely rare.

The gross pathology of adenomas is similar to that of the majority of benign tumors. They comprise a large part of the group classed as polyps or papillomas, although the sessile form is not uncommon, especially in the early stages of the tumor. They usually occur singly, but may be multiple. Such a condition is known as multiple polyposis and may be widespread in the lower part of the ileum and colon. The tumors vary in size from the tiniest filiform thread, the diameter of a pinhead, to a mass as large as an English walnut. The latter are usually recognized only when they produce obstructive symptoms. Multiple polyposis is frequently indistinguishable from colitis by clinical symptoms alone. The gross appearance differs very little from that of other types of polyps. The mucous membrane is usually intact and has a deep reddish color as a result of hyperemia. It is often convoluted and follows the outlines of the tumor, dipping into the crevices and producing a fungating appearance. On section, the tumor is a mushroom-like mass, with a central white fibrous stalk leading up from

the intestinal wall and ramifying between soft, friable masses of glandular tissue lying at the periphery. The mucous membrane can be followed by the naked eye down to the point of union with the normal mucosa of the intestinal wall.

The glandular elements of a typical adenoma show two types of cellular development. There is less proliferation near the pedicle. The cells are very similar to those of normal intestinal epithelium, with dark oval nuclei lying at the bases of columnar cells which are distended with mucus. Approaching the periphery the cells became more carelessly arranged. The nuclei are often 3 or 4 deep, the cytoplasm is granular, and nuclear polarity is lost in a cell that is not of the pure columnar shape. The nuclei may be rich in chromatin and in some places resemble malignant cells.

The connective tissue stroma is composed of ramifications of the pedicle between the glandular elements of the tumor. It arises from the submucosa of the intestine and passes up into the tumor as a well formed band of connective tissue fibers and some muscle tissue. Well formed blood vessels are found in this pedicle. Toward the periphery, the stroma consists of fibroblasts and spindle cells and is much more cellular than the base of the pedicle. There is found in the former region an admixture of small round cells, large mononuclears, polymorphonuclears, eosinophils, plasma cells and red blood cells in large numbers. As the tumor grows older the differences in the cellular elements in the pedicle and at the periphery of the tumor become more marked. Saint attributes this to properties of the cell type. He classes those near the base as mucous cells primarily, while those at the periphery are undifferentiated cells the chief function of which is proliferation.

An adenoma may be defined as benign hypertrophy of the glandular epithelium of the mucous membrane. Two theories of etiology are recognized. Saint considers them inflammatory in origin and bases his conclusions on certain features characteristic of inflammation found coincident to the tumor, such as the presence of round cell infiltration, the occasional occurrence of Oxyuris vermicularis at the base of these tumors, their development in large numbers in the presence of inflammatory conditions, such as colitis, and their frequency in locations most subject to irritation. Hauser and Bordenauer attribute the development of the tumor to a primary epithelial change. Both theories are plausible, but in the light of the material studied in this laboratory, the first receives the better support.

The process of development of adenomas has been described by Saint as occurring in certain steps. These show the stages of growth so clearly that they are quoted verbatim. 1. There is a thickening in the mucosa, caused by hypertrophy and hyperplasia of the glandular

tissue which forms an upward fold. 2. There is a thickening of the submucosa, with an upward projection that acts as the forerunner of the pedicle. 3. The passage of feces and the peristaltic movements along the bowel exert pressure and traction on the fold, drawing it

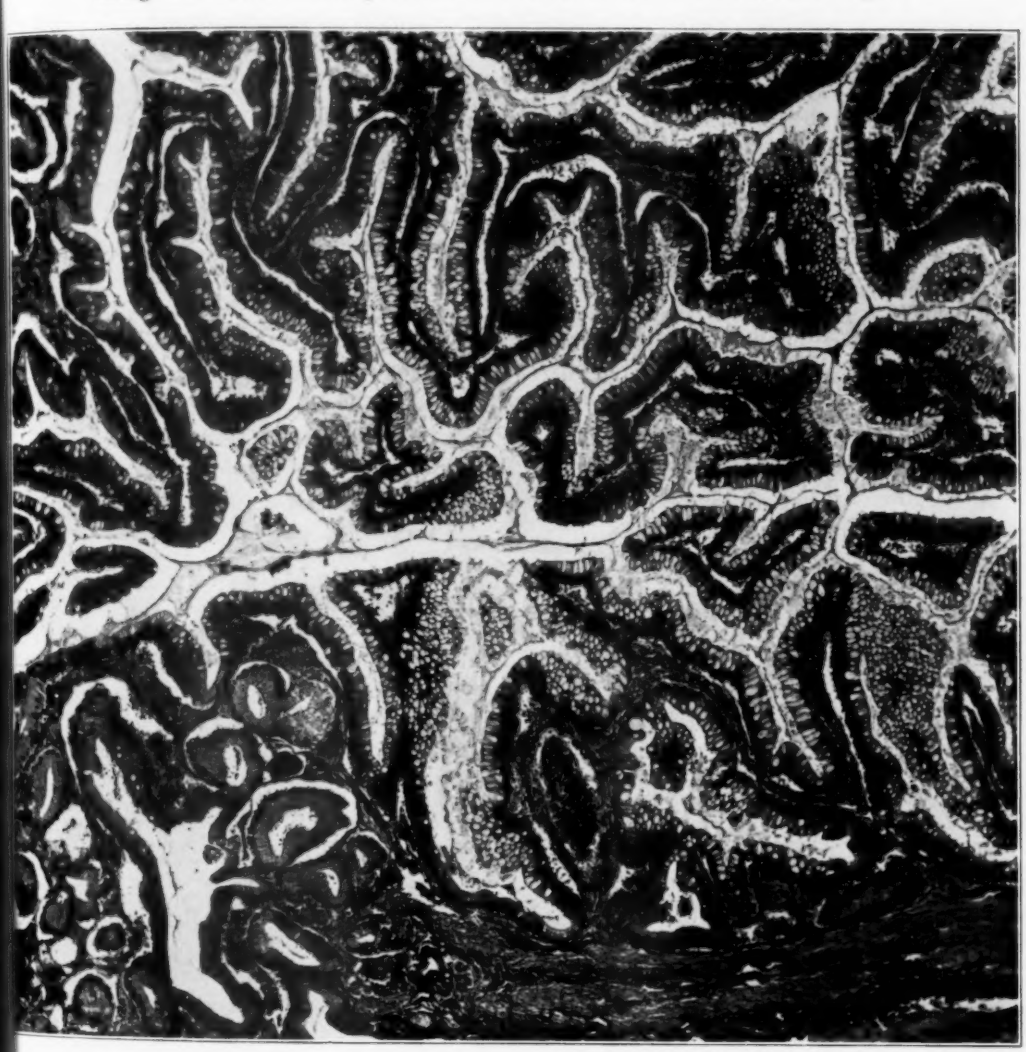


Fig. 22 (path. no. 38963, case 5).—Low power photomicrograph of a benign adenoma. Note the tortuous arrangement of the glands and the retention of the columnar cell type. Mucous goblet cells are especially numerous. There is little or no stroma.

out into the shape of the pedicle. 4. The proliferation of glandular epithelium from the center of the growth expands the head of the tumor into its mushroom form.

As a rule, the diagnosis of adenomas offers no difficulty, microscopically. These tumors are of relatively little importance clinically, except when malignant change has taken place, but for this reason must be regarded as a potential source of danger. This subject has been thoroughly discussed under the heading of adenocarcinoma.

MYOMAS

While myomas are not among the most common tumors in the small intestine, they do occur with sufficient frequency to warrant their consideration as a pathologic entity. Foerster first described this tumor in the small intestine in 1858. He found a small circumscribed nodule in the ileum opposite the mesenteric attachment which resembled closely in structure the myoma common to the uterus. Bottcher, in 1870, and Schatzler, in 1871, were the next to recognize the myoma as a definite tumor type in the intestine. Herteaux collected thirty-two cases in 1899, and in 1925 King brought the number up to forty-two. These authors found the frequency to be about equally divided between the small and the large intestines. The latter author considered the myoma to be among the three most frequent types of benign tumors, placing the incidence above that of adenomas. The figures of this series of cases, however, do not support this frequency, as only three cases were found.

Few conclusions can be drawn in regard to sex, race and age from so limited a number of cases. From data derived from collected cases, however, the decade in which these tumors are the most frequent is the fifth. Myomas have been found in persons as young as 13 and as old as 68 years. Males are more often affected than females in the ratio of 3:2.

The greatest incidence of myomas is in the ileum. Next in susceptibility is the jejunum, while the duodenum is rarely the seat of the growth. Staemmler found only 12 per cent of his cases in the duodenum.

The gross pathology of this type of tumor differs very little from that of other benign growths. Myomas may vary in size from that of a submucous nodule no larger than a pea to that of a large grapefruit or a child's head. They may grow either internally or externally, the latter type attaining the larger size. When internal, they are most commonly sessile, although the polypoid form is not rare. They are oval or round, circumscribed and feel freely movable beneath the mucous membrane, which is intact unless it has undergone pressure necrosis. They are thought to arise most frequently from the inner, circular layer of muscle, and opposite the pedicle attachment is sometimes seen a dimple-like depression in the serous surface. It is assumed

that the external tumors arise from the outer muscle layer and seldom distort the intestinal lumen, although there are exceptions to the rule. The latter may lie loosely in the peritoneal cavity, may grow retroperitoneally or in the layers of the mesentery. This form may be attached by either a broad base or a narrow pedicle.

The consistency of myomas, either internal or external is firm and rubbery. The color of the former is usually a deep red, owing to the extravasation of blood. Goldschmidt has commented on the hemorrhagic tendencies of myomas, terming them "bleeding myomas," and has emphasized the importance of melena in their diagnosis. On cut section, the tumor is bluish gray. The origin of the tumor from the muscle layer can often be traced by the naked eye.

The characteristic histologic picture of a myoma is that of benign hypertrophy of muscle fibers with an added overgrowth of fibrous connective tissue. The myomatous character is almost pure in young tumors and resembles very closely that of uterine myomas. The cellular elements consist of smooth muscle cells, rather larger than normal, but shorter and more rounded. The nucleus is larger and stains lighter than that of the normal cells. Numerous chromatin particles are present, but definite mitoses are absent. The periphery of the tumor is cellular, containing an infiltration of small round cells, plasma cells and mast cells, especially about the smaller blood vessels. The center of the tumor is frequently fibrous and grows faster than the periphery, and from this area alone can be confused with a fibroma. This feature has given rise to the mixed forms of fibromyoma and myofibroma commonly seen in the literature.

Myomas are subject to circulatory and regressive changes. Venous stasis produces capillary hemorrhages visible in the gross specimen as tiny red flecks. Occasionally, the hemorrhage becomes sufficiently large to cause pressure necrosis and cystic formation. Such a picture is regarded as a telangiectatic myoma. Hyaline degeneration is the most common regressive change, although calcification within the tumor has been reported.

So far as is known, the only possible points of origin of myomas in the intestine are the muscular layers, both internal and external, and the musculature of the arterioles. The latter source, while possible, is open to question. Certainly the most frequent source is the tunica muscularis. The three tumors of this series were definitely traced to this origin, and two of these could be seen to arise from the internal layer. Much can be said regarding the etiology, and little proved. Virchow was an exponent of the irritation theory, while Cohnheim considered the growth as a hypertrophy of misplaced germinal centers. Supporting the first theory is the somewhat general belief in irritation

as an etiologic factor in neoplastic growth. As Staemmler pointed out, however, if this were the causal factor, one would expect myomas to occur in places subject to the most irritation, and multiplicity would not be unusual. Present evidence favors the latter theory.

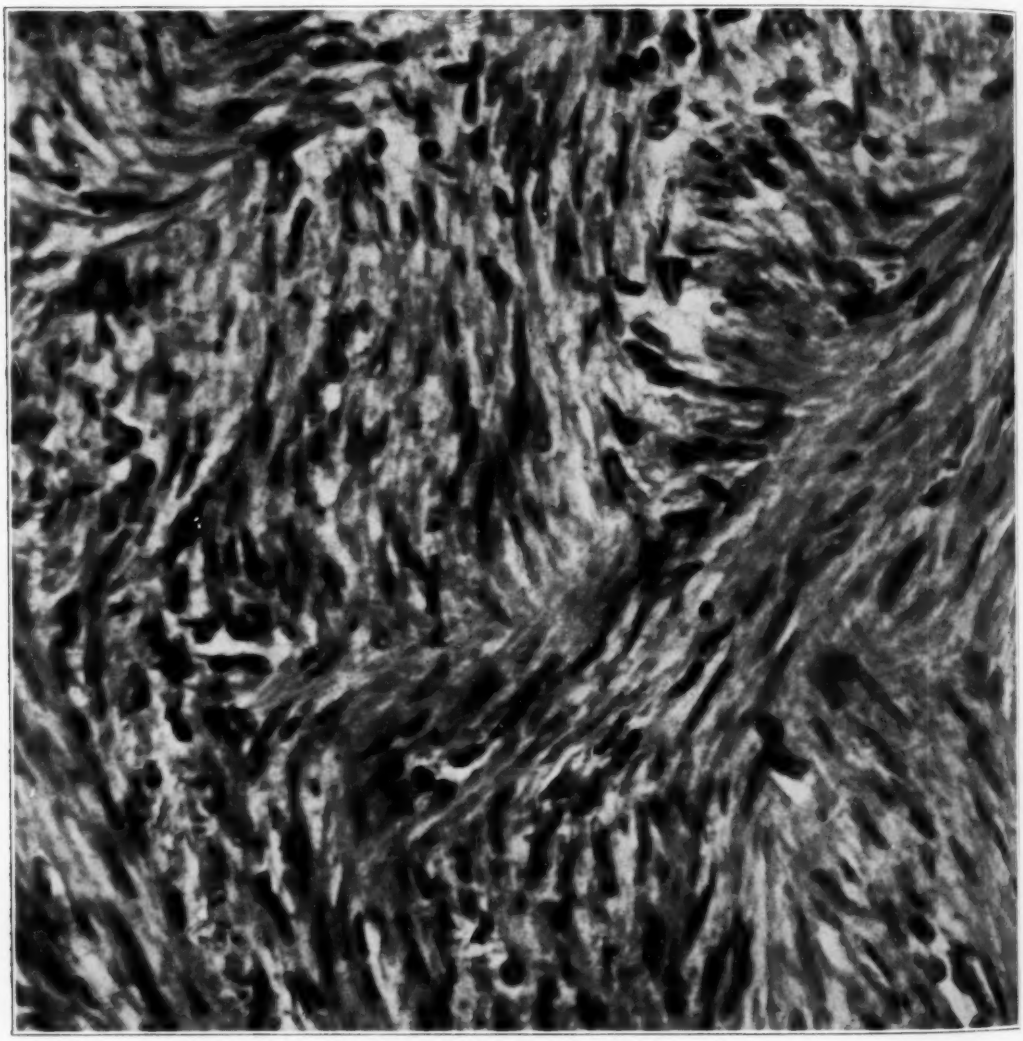


Fig. 23 (path. no. G10584, case 6).—High power photomicrograph of a myoma of the ileum (same tumor as that in figure 4). Note the elongated spindle-shaped cells containing abundant cytoplasm and oval nuclei. The cells are arranged in strands and whorls, and bear a striking resemblance to the sarcoma shown in figure 15.

The growth of this tumor is expansive in nature. It remains fairly well circumscribed, but may cause necrosis or atrophy of the sur-

rounding intestinal wall by pressure. Coincident with the expansion of the muscular element of the tumor, the fibrous stroma undergoes rapid hypertrophy, and it may be difficult to determine which tissue is predominant.

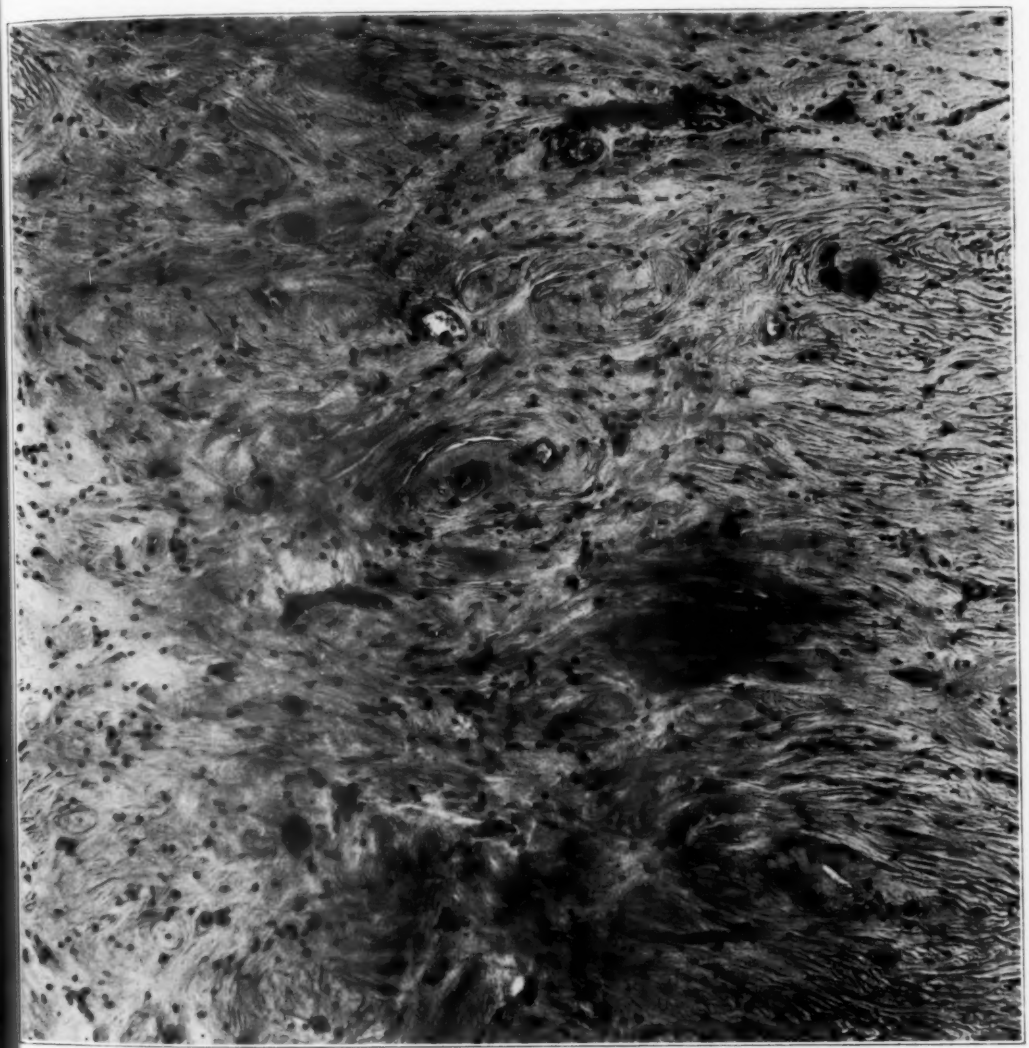


Fig. 24 (path. no. G3102).—Low power photomicrograph of a myoma of the ileum undergoing hyaline degeneration. The normal muscle cells are seen at the extreme right of the picture merging into the degenerating area. There is moderate cellular infiltration.

A word should be added in regard to sarcomatous change. The manner in which it occurs is not clear, but it is definitely known that

some myomas ultimately become malignant. The cells assume the characteristics of malignancy, and the tumor ceases to conform to the circumscribed limits of a benign growth.

FIBROMAS

Pure fibromas are among the rarest tumors found in the small bowel, but the mixed forms are much more common. Languet doubted the existence of the pure form at all. Nevertheless, thirty-nine cases, including the mixed forms, have been found in the literature that are considered authoritative. Four only were found in this series of cases. The frequency is no greater in the large intestine; in fact, most investigators of the subject consider that the fibroma holds a predilection for the small intestine.

This is a tumor primarily of advanced age. While some cases have been reported in children under 10 years of age, the majority occur in persons in the fifth and sixth decades of life. The youngest of the four patients was 52, the oldest 69 years of age. This is due in all probability to the fact that many tumors produce no symptoms and are found only at autopsy. There is no apparent racial distinction, the 4 cases being equally divided between the white and the black race. All four were in men, but this predominance is not borne out in the data from other reported cases.

The fibromas most commonly select the ileum as the site of growth, probably by reason of its greater extent. Cases are reported in the jejunum and duodenum roughly in proportion to their respective lengths.

There is nothing characteristic about the gross form of fibromas. They may grow internally as sessile or pedunculated tumors, or they may extend out into the mesentery, retroperitoneally, or they may be free in the peritoneal cavity as external tumors. Staemmler stated that the former predominate in the ratio 2:1. The mucous membrane is usually intact, but may be ulcerated and bleeding. The tumor mass is round or oval, discrete and circumscribed, and freely movable. It is firm and rubbery, and the cut section is grayish white. Some fibromas may assume a combination of the internal and the external forms and may appear as a large irregular mass which in the gross section looks malignant.

In the microscopic section, the bulk of the tumor is seen to consist of connective tissue hypertrophy and hyperplasia. It is relatively poor in cellular elements. Elastic fibrils are predominant and may be demonstrated by Weigert's stain for elastic tissue. Interspersed among these fibrils may be seen numerous spindle cells and stellate fibroblasts. The latter are more mature near the center of the tumor, with branching cytoplasm and small dark nuclei. In the younger sections at the

periphery, they contain less cytoplasm, and the nuclei are larger, stain lighter and are occasionally vesicular. There is a moderate admixture of small round cells, plasma cells and red blood cells at the periphery,

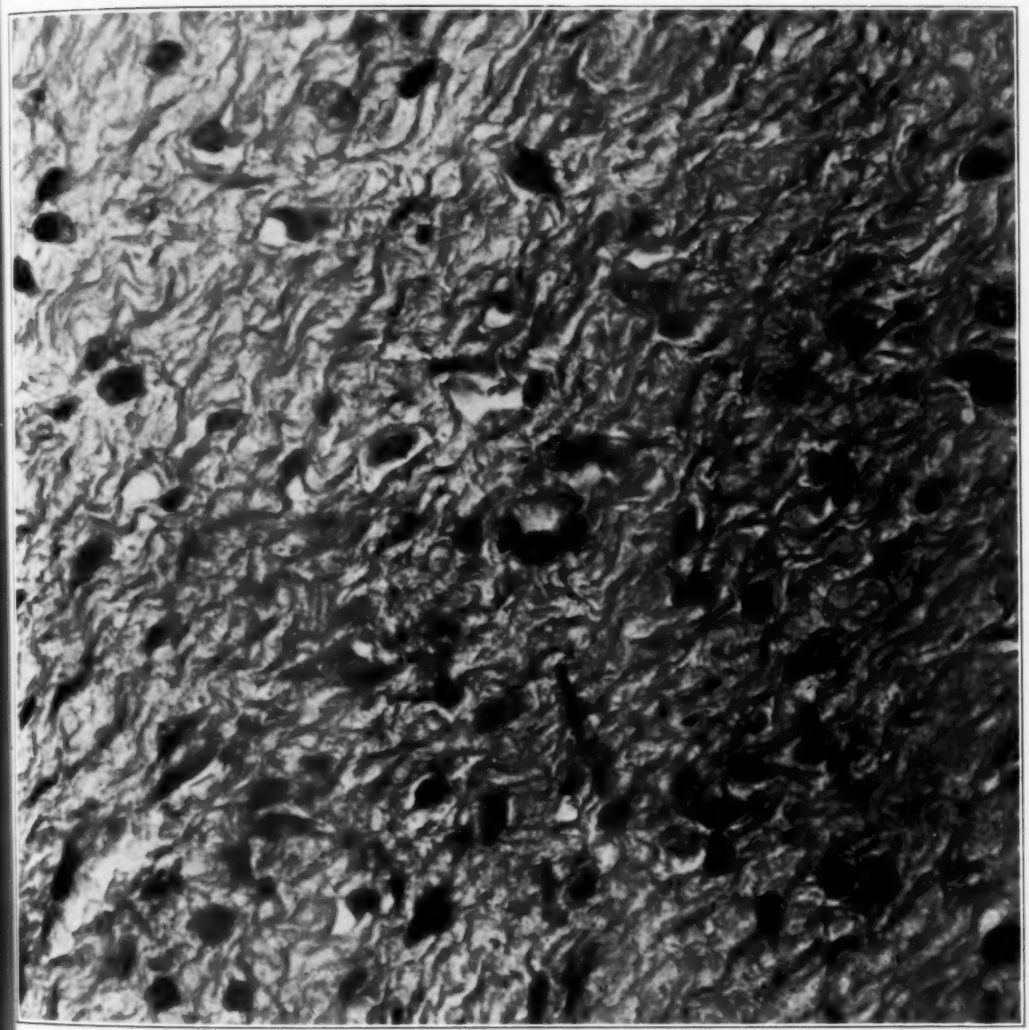


Fig. 25 (path. no. 46153, case 7).—High power photomicrograph of a fibroma of the duodenum. There is a dense overgrowth of elastic fibrous tissue among which are interspersed numerous large stellate cells with oval nuclei (case of Dr. Dean Lewis).

and in cases in which the mucous membrane is ulcerated and secondary infection has set in, leukocytic infiltration is marked.

Areas of myxomatous degeneration are not uncommon. Such an area resembles the pure myxoma in appearance, consisting of ramifying stellate cells enclosing a granular basophilic matrix. This tissue is grouped about small blood vessels, and vascularity is more marked in these areas than in other parts of the tumor.

Histogenetically, fibromas arise from connective tissue cells. The most frequent sources are the submucosa and subserosa, but periarterial connective tissue has also been considered as a possible point of origin. Herteaux considered the external form as arising chiefly from the subserosa, and the internal from the submucosa. The confusion between fibromas and myomas and the mixed forms is justified in that they often contain tissue of the two types, and it may be difficult to determine which is predominant and gave rise to the original tumor. The fibrous tissue seen in myomas is, however, of a secondary nature, and its chief function is that of a supporting stroma.

The origin of the myxomatous tissue is questionable. Some investigators regard it as an edematous form of the original fibroma. Others consider it as a specialized type of cell arising from the same tissue as the fibroma but retaining the property of secreting mucus. In either event, the presence of myxomatous tissue is of secondary importance.

ARGENTAFFIN OR CARCINOID TUMORS

The peculiar type of argentaffin or carcinoid tumor has aroused considerable discussion during recent years. Lubarsch, in 1888, first pointed out that this tumor, while resembling carcinoma histologically, was characterized by absence of metastases, lack of glandular structure and variation of the cell type from that of the normal mucosal cell. Nevertheless, he termed it primary carcinoma of the intestine. Numerous other cases were reported between that time and 1904, and the term carcinoid came to be used rather loosely to denote the resemblance to carcinoma in the absence of malignant characteristics. Trappe had stated that the origin of carcinoids could be traced to aberrant pancreatic rests which are not uncommonly found in the gastro-intestinal tract. The cells did indeed bear some resemblance to the cells of the islands of Langerhans, and the theory at that time found popular support. Bunting reported several cases in 1904 and commented on the similarity to the basal cell tumors of the skin described by Krompecher. Burkhardt agreed with this view, demonstrating the dissimilarity between carcinoids and pancreatic tissue and their likeness in clinical and pathologic respects to the basal cell tumors. Hubschmann, in 1910, suggested, in view of their yellow color, a possible origin in the chromaffin cells at the bases of the crypts of Lieberkuhn. Four years later, Gosset and Masson applied the silver impregnation method of staining to the

chromaffin cells and later to the carcinoid tumors, finding the presence of silver-staining granules. They, therefore, introduced the term "argentaffin" to apply to the carcinoids that took the silver stain. They also succeeded in demonstrating the similarity by microchemical means between these cells and cells of the suprarenal cortex.

This new conception of the carcinoids was accepted as plausible, but by no means universally. The work of these two authors was repeated by Hasegawa and Danish. Forbus reviewed all the available cases in this clinic in 1925. His article published at that date is the most complete recent work and contains an excellent historical review of the subject.

The clinical features of the carcinoids are insignificant. They rarely attain a size sufficient to cause symptoms and are rarely recognized before autopsy after death from other causes. Hence the age incidence is not characteristic. Likewise, the tumors show no predilection for either race or sex.

The majority of argentaffin tumors are located in the ileum. Five of the seven cases in this series were located in the ileum, one in the jejunum and one in the duodenum. This characteristic feature is further borne out by the great frequency of these tumors in the appendix, but one is at a loss to explain why they should select this particular region of the gastro-intestinal tract. The chromaffin cells, or cells of Kulchitzky, are, according to Maximow, scattered equally throughout the intestinal tract, and therefore offer no explanation of the fact.

The carcinoids are commonly thought to be benign tumors. During the past few years, however, several cases have been reported in which metastases had occurred and in which the malignant nature was diagnosed on this basis. One of the cases in this series was microscopically benign, but metastases had occurred to the liver and lymph nodes. The tumor was identified as a member of the argentaffin group by the silver stain. Cooke summarized 104 carcinoids from the literature and added eleven cases of his own. He found metastases in 21 per cent and concluded that malignancy is not uncommon. The author neglected to state if all of these tumors were proved to be true argentaffin tumors by the silver method of staining, however, and it is questionable if some of the so-called metastasizing carcinoids were confused with carcinoma of the medullary type, a resemblance easily appreciated by comparing figures 11 and 26.

The gross pathology of these tumors is not characteristic. They are relatively small, seldom more than a centimeter in diameter, more often the size of a pea. They may be sessile, within the intestinal wall or attached to a small pedicle. They are usually single, but may occur in groups of two or more. In one instance, two tumors were found attached

to the same stalk. The mucous membrane is usually intact, but it may be very thin and hyperemic in places. On cut section, the tumor is soft and elastic and yellow.

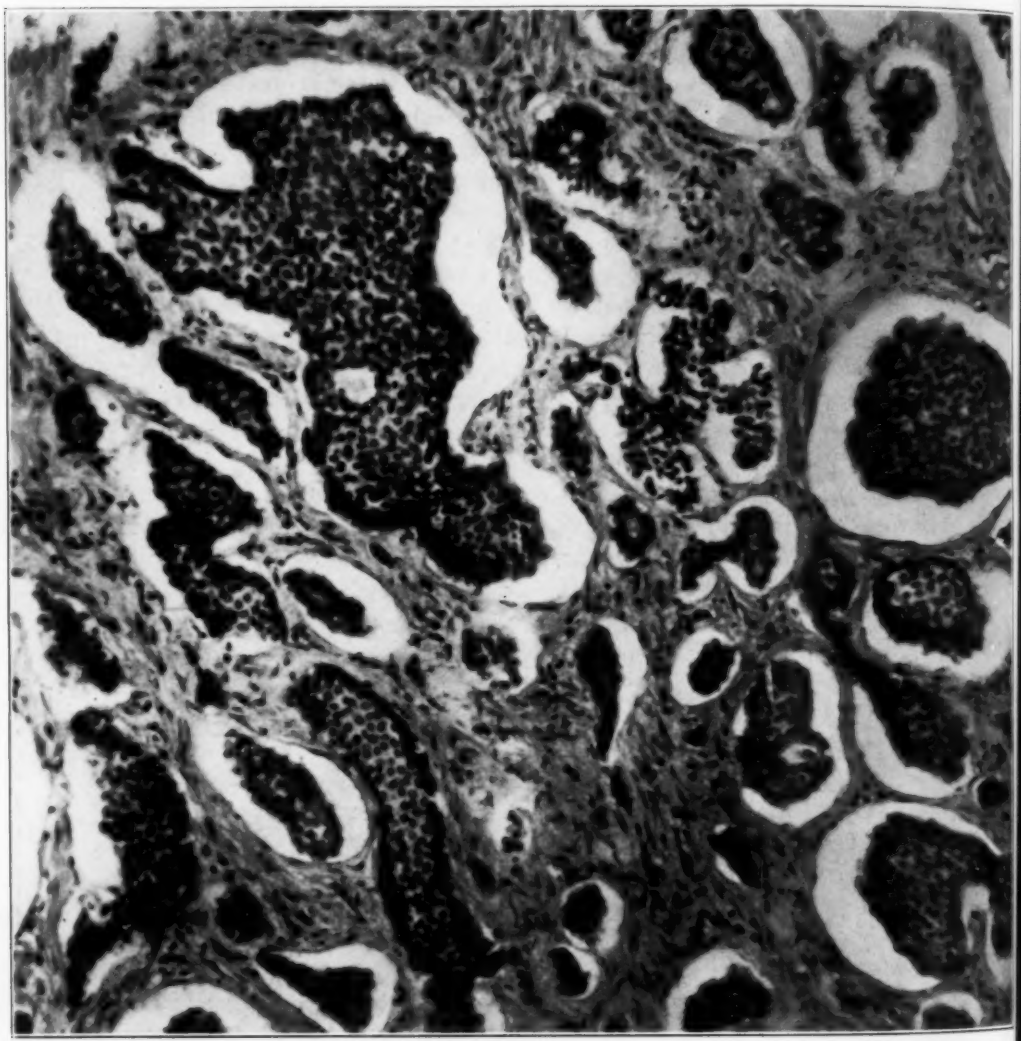


Fig. 26 (path. no. G6739, case 8).—Low power magnification of an argentaffin tumor of the ileum. The cells are small with indistinct outlines. The cytoplasm stains light with eosin, and the nuclei are small, round and dark. The cells are arranged in discrete nests with a dense connective tissue stroma. They were susceptible to the silver impregnation method of staining.

The characteristic microscopic picture is that of nests and strands of cells surrounded by a fairly definite limiting membrane and sepa-

rated by a stroma that varies in amount. The cells are small, relatively uniform, and round or oval. Near the edges of the nest of cells, pressure may cause them to assume a spindle shape. The cytoplasm

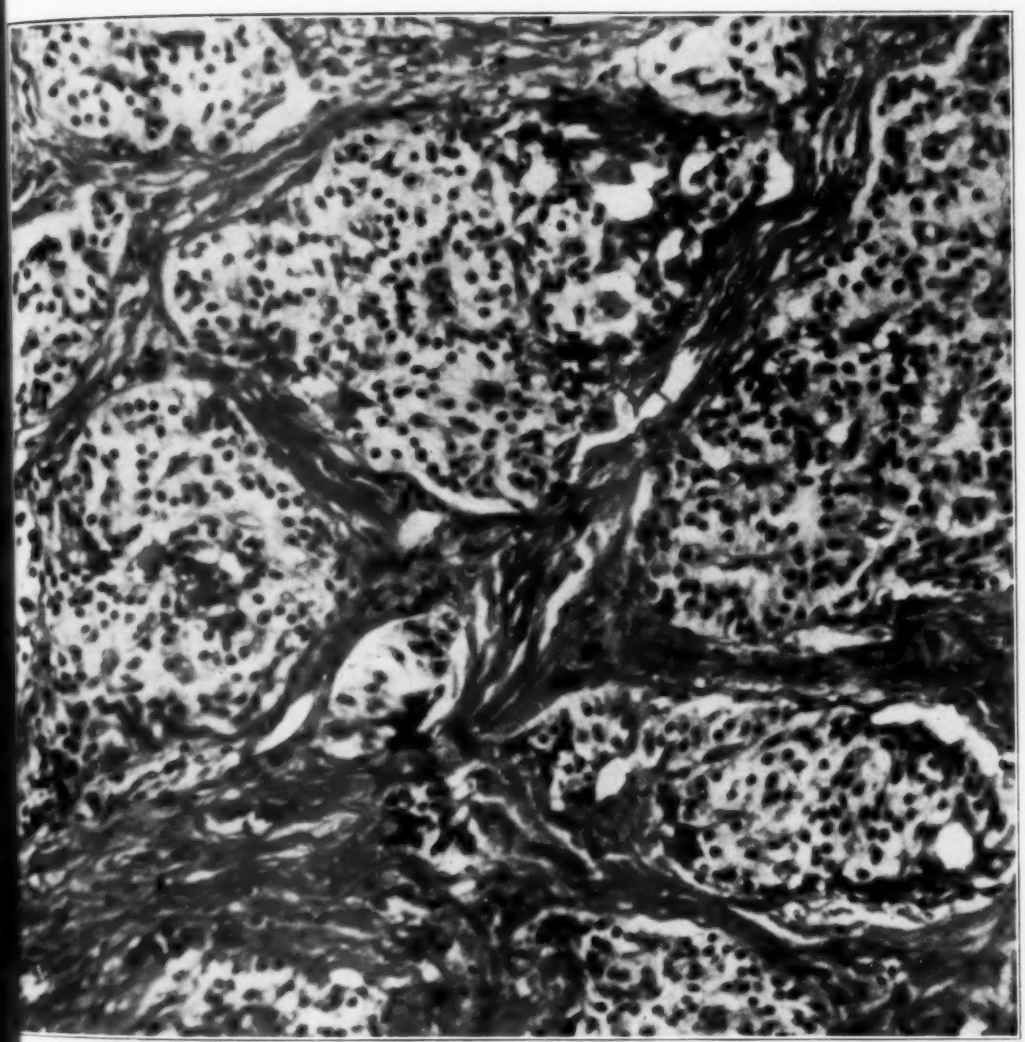


Fig. 27 (path. no. 36786).—High power photomicrograph of an argentaffin tumor of the duodenum. The cells are similar to those in figure 26, but the cytoplasm is more abundant, the cell outlines are more distinct, and a roughly alveolar formation is retained.

is pink-staining and varies in amount, in some tumors being abundant. The nuclei are rather large and conform roughly to the shape of the

cytoplasm. They take a light stain and are rich in chromatin. The stroma is formed of hyaline connective tissue in which are interspersed numerous small capillaries. Rarely, the cells assume an acinar formation, but the usual picture is that of solid sheets of cells.

Much remains to be explained regarding the histogenesis of argentaffin tumors. The theory of origin from pancreatic rests has had many adherents. Ewing classes these rests as a type of carcinoid. There are at least two features, however, that are not in keeping with this theory. The microscopic picture is definitely different in the two. The carcinoids do not show the acinar arrangement of cells characteristic of pancreatic tissue. The cells of the former, it is true, do resemble the cells of the islands of Langerhans known as the B type. Beyond that the resemblance ends. The second feature is the location. Pancreatic rests occur with greatest frequency in the duodenum, rarely in the jejunum and ileum. The carcinoids, on the other hand, are far more common in the lower part of the ileum and in the appendix, and are rare in the jejunum or duodenum.

The resemblance to basal cell epitheliomas of the skin, suggested by Bunting, is striking. So little is known regarding the origin and etiology of each, however, that it is impossible to consider them as analogous.

Forbus came to the conclusion, as a result of his study, that the endocrine theory of origin from the chromaffin or argentaffin cells was the most plausible, and in view of the present evidence, this is by far the most acceptable.

Very little can be added to the conception of these tumors from this study. The term carcinoid, although often used loosely, should not be discarded. It is a descriptive name and should be used to designate tumors that resemble the argentaffin tumors histologically. One cannot use the latter term accurately, however, until the diagnosis has been proved by the silver method of staining.

ABERRANT PANCREATIC RESTS

The aberrant pancreatic rest is a type of benign tumor growth that is of minor clinical significance. Nevertheless, it occurs with such frequency as to deserve brief consideration in any treatise on gastrointestinal tumors. The first cases reported in the literature were those of Klob in 1859. Warthin reported two cases in 1904, but neither occurred in the small intestine. The subject was reviewed in full in 1921 by Horgan. Simpson, working in this clinic in 1927, studied these tumors extensively, and his subsequent article is the most complete work of recent date. He collected a total of 157 cases from the literature, seventy-three of which were located in the small intestine.

These rests, like the preceding group of tumors, rarely produce clinical symptoms and are seldom found except at autopsy. Ages, therefore, mean little. The cases of this series were equally distributed between the sexes and races.

Assuming that pancreatic rests arise as misplaced embryonic tissue, it is logical to assume that the site of election is near the pancreas. This is borne out by the location of the tumors in this series. Two were found in the duodenum, three in the upper part of the jejunum and one near the midportion of the ileum. This distribution agrees closely with that noted by Simpson.

The tumors usually appear grossly as small submucous nodules, rarely more than a centimeter in diameter. They are irregular in shape, elongated, flattened or oval. Occasionally, they are of sufficient size to cause obstruction. One of the six cases here reported produced an intussusception of the ileum. The tissue is soft and spongy to touch, and is freely movable beneath the mucous membrane. The cut section is grayish white, and throughout the tumor can be seen irregular patches of denser tissue representing the pancreatic tissue.

The microscopic picture of pancreatic rests is essentially the same as that of normal pancreatic tissue, except for the distribution. When seen under low power magnification, the deep blue stain of the lobules stands out in marked contrast to the lighter pink interlobular connective tissue. The aberrant tissue may be scattered throughout the intestinal wall, but the largest accumulations are usually found in the submucosa. They may occur in compressed strands between the layers of the muscularis. Higher magnification shows the cells to be very similar to those of the normal pancreas. The cells are in acinar arrangement. The cytoplasm is abundant and basophilic, and zymogen granules are abundant. Normal islands of Langerhans are found in some sections, but are not constantly present, comprising one of the differences between the normal organ and the aberrant tissue. Excretory ducts lined by tall columnar or cuboidal cells are found in certain parts of the sections. Simpson has emphasized the resemblance of these ducts to adenocarcinoma in some instances.

Many theories have been elaborated to explain the development of accessory pancreatic tissue. That of Warthin is accepted at the present time in preference to the earlier theories of Zenker and Glinski. The former considered the growths as arising from lateral buds of the rudimentary pancreatic ducts as they pass through the intestinal wall in the embryo. They are thus segregated and carried either up or down as the intestine undergoes the process of longitudinal growth. Simpson observed the proximity of the ventral pancreatic bud in the embryo to the primitive yolk stalk, and believed that small buds might easily become detached at this point and be carried in either direction by the

later development of the latter structure. This theory is the most plausible offered as yet and goes far to explain the progressive infrequency of the growth toward the lower part of the intestine.

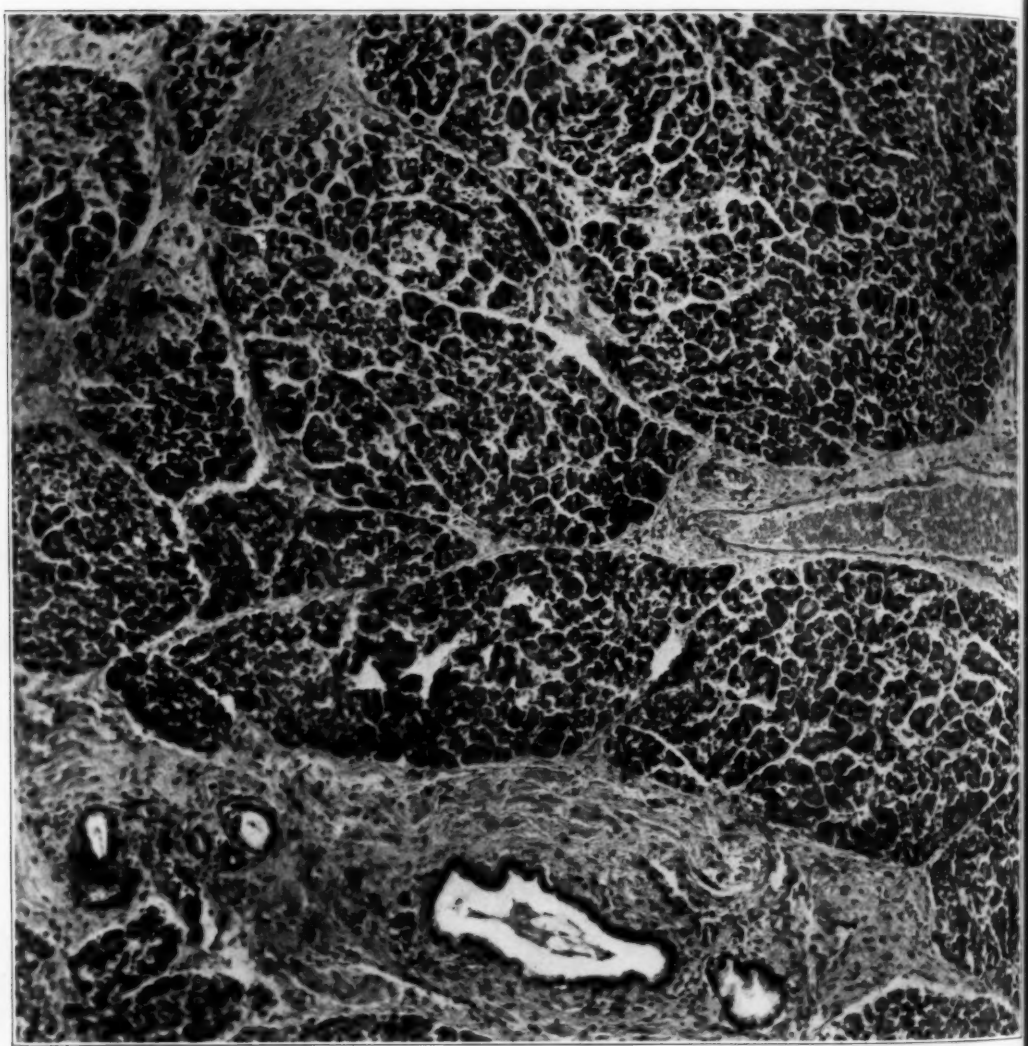


Fig. 28 (path. no. G10579).—Low power magnification of an aberrant pancreatic nodule found in the duodenum at autopsy. Note the acinar arrangement of the cells which are small and possess a granular, basophilic cytoplasm and small round nuclei. Occasional islands of Langerhans are found, and in the lower part of the photograph can be seen a dilated pancreatic duct.

The question of the relation of aberrant pancreatic tissue to diverticula of the intestine has been raised by several investigators. Koch

and Suzuki examined fifty cases of diverticulum and found pancreatic tissue at the tip of the structure in two instances. Albrecht and Arzt reported a case of Meckel's diverticulum to the end of which was attached an aberrant pancreatic nodule by a thin fibrous cord. The discovery of cases such as these has given rise to the theory that the accessory tissue existed first, and that the diverticulum was caused as a secondary result of traction on the tumor. The evidence at hand is insufficient to prove the theory, however, and it is doubtful if the occurrence is more than coincidental.

ANGIOMAS

True angiomas of the intestine are regarded by pathologists as being extremely rare in the small intestine. Herteaux was able to find only three cases. Helvestine reported a single case in 500 autopsies. Three cases are reported in this series. Two types are found, hemangioma arising from the vascular system and chylangioma arising from the lymphatic system. The latter tumors are classed variously as chylous extravasations and chylangiectases. They are commonly secondary to another pathologic process and possess little clinical significance unless large enough to cause partial obstruction of the intestinal lumen. Large hemangiomas sometimes become hemorrhagic and produce marked secondary anemia.

The clinical features of the angiomas are insignificant. No preference for age, race or sex has been demonstrated. One of the tumors was located in the duodenum, and two in the jejunum. There is no reason why the ileum should be excluded, and no doubt a larger number of cases would show an equal distribution throughout the small intestine.

Hemangiomas may be of two distinct types. The simple form consists of hypertrophy and overgrowth of the small blood vessels. The cavernous type shows in addition, large, dilated, blood-filled cavities and sinuses. Chylangiomas show the same types and in addition a more dilated form termed cystic, in which the supporting tissue tends to become atrophic. Multiplicity occurs in a large number of cases. Two of the three cases consisted of multiple nodules scattered along their respective channels of supply.

The gross appearance of the tumors differs slightly. Hemangiomas are small, reddish, submucous nodules, rarely more than a centimeter in diameter. The mucosa is seldom broken, but is hyperemic, and bleeding from the tumor is not uncommon. On section, the cut surface of the tumor is red, and blood may be squeezed from the interstices, leaving a porous spongelike mass. Chylangiomas, on the contrary, are grayish or yellow and softer, and on squeezing, a clear yellow or milky

fluid is expressed. Section reveals the tumor composed of cystic dilatations of varying size separated by thin septums or spongy tissue according to the individual case. The smaller nodules may not be visible to the eye, but can be recognized by palpation. The larger tumors may cause a prominence on the serous as well as on the mucosal surface.

The characteristic microscopic picture of simple hemangiomas is an overgrowth of blood vessels. These are small and are arranged in tortuous masses or whorls. The capillary walls are composed of large endothelial cells, shorter and more plump than normal, with large light nuclei, and may be two or three layers deep. The vessels are separated by a connective tissue stroma which may or may not be densely infiltrated with cells of the myeloid and lymphoid series. The cavernous type consists of large blood-filled spaces which are lined with a single layer of endothelial cells. The cystlike structures may be filled with fibrin in old tumors. The septums are thin and composed of a scant connective tissue in which may be interspersed a few muscle fibers. The cavities are smaller near the edge of the tumor, and, in fact, one often recognizes both types of angioma in the same section. The simple form is predominant near the borders of the tumor, with dilatation increasingly greater near the center of the growth.

Chylangiomas are very similar in appearance. The new growth can sometimes be seen arising from and continuous with the lymphatic channels. The cystic spaces are larger, as a rule, and, instead of blood cells and fibrin, they contain a gelatinous pink-staining material through which are scattered a few leukocytes and epithelial cells.

The histogenesis of the angiomas remains somewhat confused. Jordan described three plexuses of blood vessels in the intestinal wall. These are the submucous, intermuscular and subserous. There are thus three possible sites of origin, although, judging from the customary location of the tumor in the submucosa, the first is by far the most common. Rokitansky considered the growth as a mere hypertrophy and overgrowth of vessels. Virchow contended that irritation and trauma were largely responsible for this phenomenon. Thoma, while accepting these factors to a limited extent, felt that hypertension combined with weakness of the vessel walls played an important part in the process.

Chylangiomas are thought to arise from the lymphatic plexus in the submucosa into which the lacteals of the villi empty. Two theories of etiology have been offered. Many writers believe that the tumor develops from misplaced embryonic tissue, but evidence to support this is lacking. That the cause is stasis and back pressure brought about by blockage of the mesenteric glands seems more plausible. The cystic appearance of the tumor is more suggestive of a dilatory process than a hypertrophy. Such cases are so rare that a comprehensive study of the subject is difficult.

Hematomas are not true tumor growths, and are mentioned with angiomas only in view of the fact that symptoms are sometimes produced resembling those of other tumors. They are extremely rare, and no mention of hematomas of the small intestine as a clinical or pathologic entity has been found in the literature. They are apparently purely mechanical in origin, consisting of an intramural extravasation

Fig. 29 (path. no. 24867, case 10).—Low power photomicrograph of a hemangioma of the ileum. The tumor has grown outward in fungating polyps composed largely of hypertrophied capillaries. They are covered in part by epithelial cells, and there is a dense infiltration of small round cells throughout. Note the normal mucosa in the lower right corner.

of blood, without any evidence of cellular hypertrophy. The etiology is not known. Hypertension, together with pathologic weakness of the vessel wall due to trauma, irritation or necrosis are factors to be considered. One case was found following postoperative mesenteric

thrombosis. It is conceivable that the stasis and back pressure caused by the blockage of the vessel brought about the rupture of the vessel.

These tumors have little clinical significance, unless the extravasation is sufficiently large to cause a partial occlusion of the intestinal lumen.

Fig. 30 (path. no. G9819, case 11).—Low power photomicrograph of a hematoma of the ileum causing partial obstruction. The organized blood clot has split apart the longitudinal fibers of the muscle coat and the submucosa in a fan-shaped manner. There is moderate leukocytic infiltration.

This was the condition brought about in one of the cases here reported. Both cases occurred in elderly white men, one aged 77 and the other

78 years. The condition may possibly be related to old age. Both tumors occurred in the ileum, but any part of the small intestine is susceptible.

The gross appearance of the tumor is that of a smooth oval or rounded semispheroid mass in the intestinal wall, lifting the mucosa and projecting into the lumen. Both cases were internal, although tumors of the external type can arise in the same manner, especially if the hemorrhage occurs in the subserous plexus. The mucosa may be intact at first, but later it may become gangrenous and necrotic from the effects of pressure. The tumor itself is hard and firm after the blood has clotted and organized. The cut section is dark red or black, resembling a fresh clot or an organizing thrombosis.

Very little can be seen in the microscopic section except a typical blood clot. Depending on its age, this may be fresh red cells with strands of fibrin or, if older, laminae of platelets with bordering accumulations of leukocytes with intervening strands of fibrin. The tumor is not encapsulated, but infiltrates and splits apart the normal tissues, in some places causing atrophy and necrosis. There may be a moderate round cell infiltration about the edges, if the condition has existed for any length of time.

LIPOMAS

Small, soft yellow nodules are not infrequently found in the small intestine at autopsy, which are found on histologic examination to be lipomas. They are by no means rare, but seldom cause symptoms before death results from other causes. Odelberg reported thirty-three cases, found in the literature, in his review of the subject and stated that 25 per cent of all intestinal lipomas occur in the small intestine. Seven cases are reported in this series, comprising 8 per cent of the total.

This type of tumor is of minor clinical significance for two reasons. The rate of growth is very slow; from three to five years are necessary for it to attain a size sufficient to cause symptoms. In the second place, it seems a peculiarity of the tumor that it is attached by a long slender pedicle which frequently is broken, permitting the tumor to be passed per rectum. Nevertheless, lipomas on some occasions reach a large size, and, if internal, produce intussusception with its concurrent symptoms. If external, they may attain the size of a child's head, though such cases are extremely rare. None of the six cases here reported gave symptoms or were recognized before death. The occurrence of lipomas in elderly people indicates nothing more than the fact that death of the patient is usually brought about by causes other than the tumor. White men are apparently most susceptible, but there is no

explanation for this fact. There is nothing significant in the location of the tumors, as they are evenly distributed throughout the intestine.

Lipomas occur singly as a rule, but not infrequently from six to eight tumors are found in a single patient. Multiple lipomatosis is

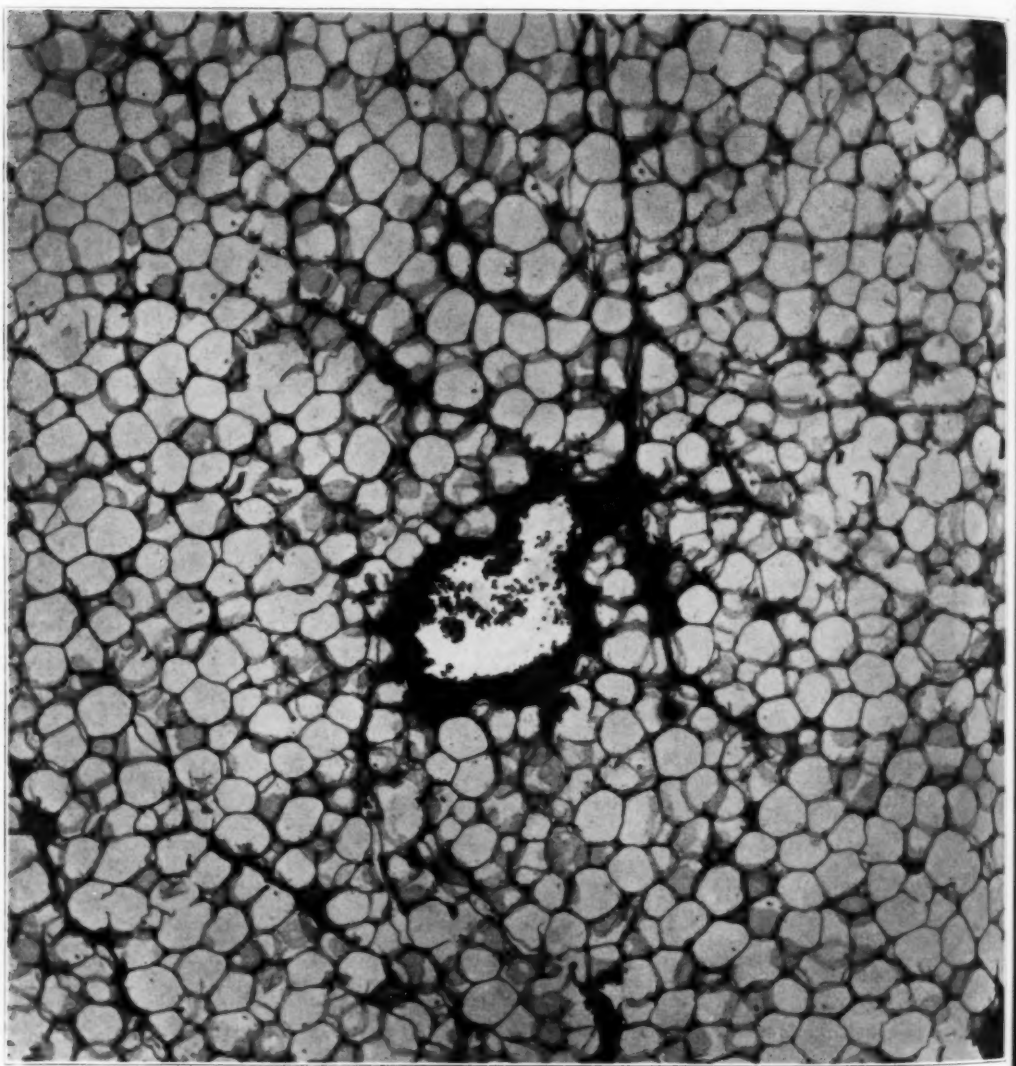


Fig. 31 (path. no. G5865).—High power magnification of a lipoma of the ileum found at autopsy. The large, polyhedral fat cells are transparent and separated by delicate fibrous septums. A large arteriole can be seen in the center of the picture.

rare. Eighty-five per cent of the tumors were internal in type. They rarely assume a size of more than from 1 to 2 cm. in diameter. They are

soft to touch and light yellow. They may be sessile in the younger stages, but tend to become pedunculated as they grow older, attached by a slender, delicate thread that is easily broken by the traction of the passing intestinal contents and peristaltic movements. The mucous membrane is intact unless ulceration has resulted from secondary infection. The cut section is yellow and resembles normal fatty tissue found elsewhere in the body.

Microscopically, intestinal lipomas are similar to those found elsewhere in the body. The cytoplasm of the fat cells is abundant and takes a very light stain. The nuclei are situated near the periphery and are small, oval and take a dark stain. The cells near the center of the tumor tend to be larger than those at the periphery. They are separated by thin septums of connective tissue, and occasional fibroblasts are found at the junction of 2 or more septums. Vascularity is not marked, but fine capillaries may be found in the interstices. The tumor is a composite growth, and, while it has no definite limiting membrane, it is sharply delineated from the surrounding tissues. It is not an invasive growth, evidently starting about a central nucleus and expanding concentrically. Round cell infiltration may or may not be present near the edges of the tumor. Hemorrhage resulting from necrosis has been observed as a secondary change and, when present, is recognized by the presence of occult blood in the stools.

A smaller cell type of tumor has been described which resembles the xanthomatous type. It is termed lipoblastoma, but is difficult to demonstrate.

The origin of lipomas in the intestine is thought to be from areolar tissue in the submucosa or, in some instances, from the subserosa. The etiology is uncertain. Staemmler regarded them as arising from heteroplastic fatty tissues, while Erlich considered the growth as a simple hyperplasia of fat cells. Odelberg suggested the contributing factor of stagnated intestinal contents, but this is at best hypothetic. The large external lipomas arising from the subserous areolar tissue are thought by some to have a prototype in the appendices epiploica.

(*To be Concluded*)

Fiftieth Anniversary of the Removal of the Gallbladder

CARL LANGENBUCH—"MASTER SURGEON OF THE BILIARY SYSTEM" 1846-1901

BÉLA HALPERT, M.D.
NEW HAVEN, CONN.

> Carl Langenbuch, der die Ektomie erfand und für die Ausführung der Choledochotomie, Choledocho-Duodenostomie und Cholangio-Enterostomie ganz genaue Anleitung gab, verdient den Namen "Meister." . . . Langenbuch hat in der Chirurgie der Gallenwege überhaupt alles ersonnen, was zu ersinnen war, und so ist es bisher diesem einen Meister geblieben.—*Hans Kehr, 1913.*
>
> (Carl Langenbuch, who first devised ectomy and who gave detailed instruction for choledochotomy, choledochoduodenostomy and cholangioenterostomy, deserves the name "master." . . . In the surgery of the biliary passages Langenbuch has thought out everything that was to be thought out, and so far he has remained the only master.)

In the surgical clinics, all over the world, operations on the biliary system are of almost daily occurrence. Thus, it is strange to realize that the first cholecystectomy in man was performed hardly half a century ago. It was Carl Langenbuch, the chief of the Lazaruskrankenhaus in Berlin who, on July 15, 1882, removed surgically a diseased gallbladder with its calculous content and thus effected a miraculous cure of a patient long incapacitated by his painful ailment of chronic cholecystitis and cholelithiasis. The approaching fiftieth anniversary of this operation seems a fitting occasion for inquiring into the life of the man and an opportunity for paying tribute to the memory of the physician whose ingenuity and courage rendered the biliary system accessible to surgery. The writings of Carl Langenbuch and the necrologies written mostly by personal friends of his are a rich store of data about his personality and character. And thus, though distant from the available local sources of information and from his still living contemporaries, it is possible to gain a fair acquaintance with Langenbuch and to view him at the most outstanding periods of his career.

From the Department of Surgery, Yale University School of Medicine.

Carl Johann August Langenbuch was born on Aug. 20, 1846, in Kiel. Here he attended the local Gymnasium, and in 1865 enrolled in the University of Kiel to study medicine. He graduated from this university in 1869, with a dissertation on ruptures of the aorta, obtaining the degree of doctor of medicine at the age of 23. Summoned for military service, he took an active part in the war between Germany and France. Being intensely patriotic, he retained a deep interest in warfare and in all medical problems connected with it. On his return from this war, he became Wilms' assistant for two years (1871-1873) in the Krankenhaus Bethanien of Berlin, acquiring there a surgical training. Langenbuch's opportunities came early and while he was still rather young. His reputation grew steadily from the date of his appointment as director of the newly organized Lazaruskrankenhaus (1873) until his untimely death on the night between June 8 and 9, 1901, at the age of 55.

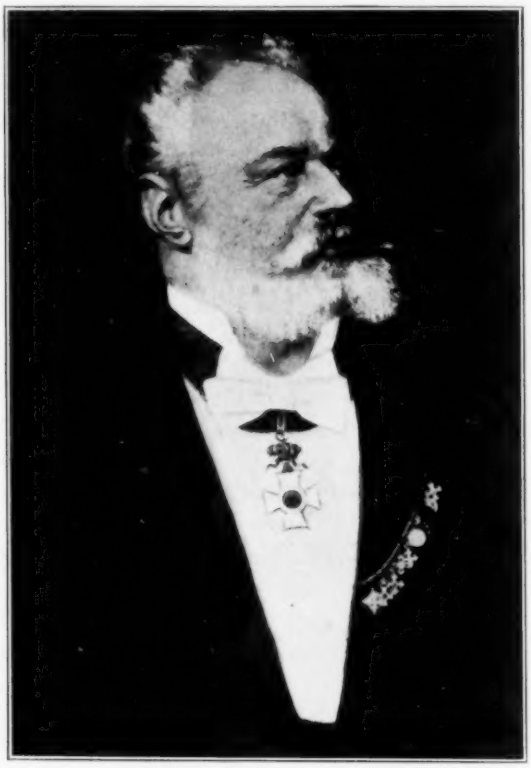
As director of the Lazaruskrankenhaus in Berlin, Langenbuch was head of both the medical and the surgical divisions, a singularly advantageous position for creative work for a man of his ability and training. A glance at the list of his publications proves sufficiently that he made the best of this opportunity.

Among the members of the German Surgical Society, the name of Carl Langenbuch appeared for the first time on the list of those present at the Third Congress, held in 1874. Although he attended each subsequent year, it was not until the Eighth Congress that his name appeared on the program. In the first session of this congress, April 16, 1879, Langenbuch discussed Langenbeck's paper on pharyngotomy, suggesting that the epiglottis be utilized to close the entrance to the larynx in order to eliminate retching and the danger of aspiration pneumonia. In the subsequent session he demonstrated a huge urinary calculus which was removed from the bladder at necropsy of one of his patients, and also the organs of a 70 year old man with situs inversus.

At the Ninth Congress (1880) Langenbuch had a variety of specimens to show: a bony tumor that he had successfully removed from the orbit of a young woman; peculiar, large concretions, one of which was removed by tenterotomy from the jejunum, and two more discovered at necropsy of a man who died shortly after operation; joint mice of traumatic origin, removed from the knee joint of a train clerk; the stomach of a 19 months old child on whom nine months previously a gastrostomy had been performed because of stricture of the esophagus; the specimen from a young woman who had a carcinoma of the stomach and on whom he performed a duodenostomy, the very first such operation ever performed.

At the Tenth Congress (1881) Langenbuch presented a brief history of two patients in each of whom, because of disabling symptoms of

wandering kidney, right nephrectomy was performed by the then customary transperitoneal approach with the modification of carrying the incision along the lateral margin of the rectus muscle instead of in the median line as was the practice at that time. He also gave the history of two other patients in whom lesions of the spinal cord were treated by nerve stretching. In the discussion Langenbuch remarked that he had



Carl Langenbuch

stretched the sciatic nerve in twenty-four cases with beneficial results. At other sessions of the same congress he discussed Zeller's paper, making mention of the fact that he performed a total extirpation of the larynx in an old woman some two years previously. He also showed two patients: one, with a chronic empyema, in whom he had removed

portions of the fifth to ninth ribs, from 5 to 12 cm. in length, and another in whom he had sutured a fractured patella.

At the Eleventh Congress (1882) Langenbuch discussed the papers by Credé and by Thiersch. He mentioned removal of the spleen in a 16 year old girl, the indication being gradual enlargement of this organ to such a size that it occupied three fourths of the abdominal cavity, causing pain and respiratory embarrassment. The patient died of hemorrhage. In the discussion of Thiersch's presentation, Langenbuch remarked that he had seen ectopy of the urinary bladder in a 75 year old man, and that he had performed operations for this condition in two 5 year old boys.

His presentations at these congresses and before the Berlin Medical Society and the ever-increasing number of his publications show his interests, the variety of cases with which he had to deal, his scientific attitude and his daring pioneer spirit. By 1882 the "Dirigierender Arzt" of the Lazaruskrankenhaus was undoubtedly a success, yet greater things were to come. Moved by the sufferings, by the futility of medical treatment, and by the loss of several of his patients with cholecystitis and cholelithiasis, Langenbuch was determined to try surgical measures. After much deliberation, animal experimentation, and studies on the cadaver, he became convinced that removal of the gallbladder would not present real technical difficulties and should lead to a permanent cure. When the occasion arose he put the matter up to the patient frankly. A few days later the patient returned, asking him to operate, and the first cholecystectomy in man was thus performed, on July 15, 1882. While such an operation seemed a daring excursion to all his contemporaries, his success proved that his preparedness more than qualified him to plan and execute such an undertaking.

In April of the following year, at the Twelfth Congress of the German Surgical Society, Langenbuch appeared with the third patient whose gallbladder he had removed successfully. He closed his presentation with the suggestion that the gallbladder should be removed not because it contains gallstones but because it forms them. His name and fame spread as others followed his steps.

A most remarkable event, and perhaps a real turning point in Langenbuch's life, was his trip to Sophia during the Balkan war. He organized and headed a voluntary medical aid expedition under the auspices of the central committee of the Red Cross. The expedition left in November, 1885, and returned in January, 1886. The story of the expedition is delightfully narrated by Langenbuch in a series of articles entitled "Kriegschirurgisches aus der Bulgarei." One seems justified in assuming that it was this service to the "Vaterland" which brought him his first official recognition: He became "Sanitätsrat."

By the time of the Eighteenth Congress (1889) of the German Surgical Society, Langenbuch had performed twenty-four cholecystectomies with results far superior to those of any of the other operative measures employed. The first volume of his "Chirurgie der Leber und Gallenblase" was published in 1894. At the Twenty-Fifth Congress (1896) Langenbuch presented a historical sketch of the development of surgery of the biliary system, an already definitely established new field in surgery. In 1897 the second volume of the "Chirurgie der Leber und Gallenblase" appeared, and with this, Langenbuch completed a lasting monument to himself.

In the "Freie Vereinigung der Chirurgen Berlins," Langenbuch was a prominent figure. He was secretary and president. At the meeting of March 11, 1901, he presided, and delivered his last address before this society. He spoke on the surgical treatment of generalized peritonitis. This was followed by a stormy discussion. On the night of June 8 and 9, 1901, Langenbuch died of generalized peritonitis following appendicitis.

Langenbuch was a stout-hearted patriot, proud of his profession, a friend of all about him, a lover of music and company, and the possessor of a deep sense of humor. He was an indefatigable, enthusiastic worker, daring, yet thorough and reliable. His presentations were always objective, to the point and dignified, yet simple and clear. He was a good physician, with much diagnostic ability, a versatile and dextrous operator who was alert, yet conservative. Langenbuch belonged to the group of surgeons who *made* modern surgery and who broadened its field with much success. From start to finish he remained the beloved "Dirigierender Arzt" of the Lazaruskrankenhaus which grew with his increasing reputation. Medical historians have yet to discover that Geheimer Sanitätsrat Professor Doctor Carl Langenbuch was one of the greatest pioneer masters of the craft and art of modern surgery.

OSTEOMYELITIS OF THE JAWS

ABRAHAM O. WILENSKY, M.D.
NEW YORK

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INTRODUCTION

The subject of osteomyelitis of the upper and lower jaws is very large and complicated. In this communication the general and anatomic considerations pertaining to this subject will first be discussed. Thereafter, the odontogenous origins and associations of osteomyelitis of the upper and lower jaws will be considered. Then the clinical and pathologic groupings of all cases of osteomyelitis of the upper and lower jaws will be distinguished and separated one from the other. In each of these groups the principles of the pathogenesis and pathology of osteomyelitis in general as described in previous studies will be

incorporated as they apply to each of the groups segregated, and the extraordinary phenomena associated with the various varieties of osteomyelitis of the superior and inferior maxillae will be shown to be caused by the anatomic peculiarities of the bony structures involved as well as of the vessels furnishing the blood supply of the bones in question. Lastly, certain points in differential diagnosis will be discussed, and the communication will be terminated by a résumé of the principles of treatment for osteomyelitis as they apply to lesions in the jaw bones.

This communication will include no case of tuberculous, syphilitic, actinomycotic or other generally similar type of infection.

REVIEW OF THE LITERATURE

There is an extensive literature on the subject of osteomyelitis of the jaws. The bulk of it is in the English, German and French languages. The largest literature is apparently in French; a number of dissertations on this subject are very extensive, but in the light of present knowledge, they do not furnish a sufficiently modern conception of this disease. The literature divides itself into four groups: One of these, the smallest, deals with osteomyelitis of the jaws proper. The second is found in the files of the dental journals and consists mostly of case reports in which the descriptions contain numerous references to osteomyelitis of the jaws usually made in a most unsatisfactory way and with inadequate or incorrect conclusions. The third deals with osteomyelitis of the jaws in nurslings and infants, of which the best descriptions are found in the German literature. A fourth group contains cases of necrosis of the jaws associated with poisoning by some of the heavy metals or with some special forms of disease as the leukemias. As it would be impossible to review adequately all of this in the space allowable for this purpose, no attempt is made to do so; references to the important communications pertaining to the subject will be made throughout this paper as the occasion arises.

The general impression one gains from reviewing all of the literature is twofold: 1. Emphasis is placed to the largest degree on the dental conditions with which osteomyelitis of the jaws is so commonly associated; however, the correct relationship of the tooth infection to the infection in the jaw bones proper is frequently not clearly stated or understood. 2. The group that occurs in nurslings and infants is more or less isolated from this general subject and is treated as if it were some independent and peculiar disease. A large literature has grown up around the subject of osteomyelitis in nurslings and infants, and, as will be pointed out subsequently, the numerous theories embodied in these numerous reports have served only to complicate the discussion. This communication will attempt, among other things, to put both of these phases of osteomyelitis of the jaws on a scientific basis.

FREQUENCY

Osteomyelitis of the jaws is a very common ailment. The jaw bones are approximately the eighth in frequency to be affected with osteomyelitis, the order of frequency, as given by Leibold (*Journal-Lancet,* 1925), being as follows: femur, tibia, humerus, radius, ulna, vertebrae, os calcis and mandible.

Hauenstein quoted Trendel as having found involvement of the mandible 24 times and of the maxilla 4 times in 1,279 cases of osteomyelitis of all the bones.

In the last seven years (1924 to 1930, inclusive) there have been treated at Mount Sinai Hospital 450 patients with acute and chronic osteomyelitis of all kinds and of all the various bones of the body. Osteomyelitis occurred in the upper and lower jaws in 39 instances; 8 cases occurred in the upper jaw, and 29 cases occurred in the lower jaw; in 2 instances it was not clearly stated which jaw was affected. This frequency corresponds to the usual experience.

SEX AND AGE

In the Mount Sinai series, 23 cases occurred in males as opposed to 16 cases in females. The usual ratio of males to females as given by most authorities is 3 : 1.

In this series the age distribution of the cases was as follows:

Up to 5 years	2 cases
10 to 20 years	9 cases
20 to 30 years	10 cases
30 to 40 years	12 cases
40 to 50 years	9 cases
50 to 60 years	2 cases

These figures refer only to hospitalized patients. In the outpatient department there are a great many more cases, and my impression is that the majority are in children.

Cases of osteomyelitis in children are no different essentially from those arising during puberty or in later life. The cases occurring in nurslings, as will be shown later, owe their peculiar clinical course merely to the anatomic location of the causative lesion, to the relatively large extent of the consequent necrosis and to the extreme youthfulness of the patient; otherwise, they are exactly similar in their pathogenesis and pathology to other cases of osteomyelitis in older children and adults. No distinction should be made, therefore, between very young children and older children, or even between children and adults. This applies with especial force to odontogenous cases. The only thing to be said is that in younger subjects the bone has more spongiosa than in older subjects or in adults, and as long as there is growth there is a

greater supply of blood and lymph; therefore, a hematogenous or odontogenous osteomyelitis may and does occur more frequently the younger the subject.

The condition occurs at all ages, not any particular age being especially liable. Osteomyelitis of a definite bacterial origin, however, is more prevalent in childhood and adolescence. In young children osteomyelitis of the upper jaw is much more frequent than that of the lower jaw, while in older children this difference no longer exists. As a matter of fact, however, ordinarily, necrosis of the lower jaw occurs oftener than that of the upper jaw because of the very much more dense bone in the lower and also because of the difference in the blood supply.

ANATOMY

The anatomy of the superior and inferior maxillae is well understood. A detailed description of the anatomy of the upper and lower maxillae will not be made in this communication, nor is it necessary for the purposes of this study. Suffice it to say that the superior maxilla is one of the irregular bones of the body, has intimate relations with the cavities of the mouth, the nose and the orbit, and contains within its interior one of the accessory sinuses of the nose, the antrum of Highmore.

In all of its peculiarities the superior maxilla resembles very much, both in its anatomic structure and in its biologic and physiologic characteristics, a vertebra of the spinal column. This resemblance is especially marked in relation to the subject of osteomyelitis.

The inferior maxilla, for practical purposes, consists of two long bones joined together at one extremity, the point of juncture forming in the completed structure the center of the bone and the apex of the chin. Each half, as well as the completed bone, functions structurally as a long bone. Each half is bent also at its center at a right angle to form the angle of the jaw on either side; the free extremity at either end helps to form and enters into the temporomaxillary articulation.

DEVELOPMENT

According to Gray, the superior maxilla commences to ossify at a very early period, and ossification proceeds with great rapidity, so that it is difficult to ascertain with certainty its precise number of centers. It appears, however, probable that it is ossified from four centers, which are deposited in membrane: one which forms that portion of the body of the bone that lies internal to the infra-orbital canal, including the floor of the orbit, the outer wall of the nasal fossa and the nasal process; a second which gives origin to that portion of the bone that lies external to the infra-orbital canal and the malar process; a third

from which are developed the palatine process posterior to Stenson's canal and the adjoining part of the nasal wall, and a fourth for the front part of the alveolus which carries the incisor teeth and corresponds to the premaxillary bone of the lower animals. These centers appear about the eighth week, and by the tenth week the three first-named centers have become fused together and the bone consists of two portions, one the maxilla proper and the other the premaxillary portion. The suture between these two portions on the palate persists till middle life, but is not to be seen on the facial surface. This is believed by Callender to be due to the fact that the front wall of the sockets of the incisor teeth is not formed by the premaxillary bone, but by an outgrowth from the facial part of the superior maxilla.

The antrum appears as a shallow groove on the inner surface of the bone at an earlier period than any of the other nasal sinuses, its development commencing about the fourth month of fetal life.

There are three stages in the development of the antrum of Highmore: (1) the formation of the anlage of the sinus inside of the cartilage capsule; (2) atrophy of the cartilage, and (3) the formation of a shell of bone around the anlage of the sinus and the beginning of secondary pneumatization. The sockets for the teeth are formed by the growing downward of two plates from the dental groove, which subsequently becomes divided by partitions jutting across from one to the other.

According to Gray's "Anatomy":

> At birth and during infancy the diameter of the superior maxilla is greater in an antero-posterior than in a vertical direction. Its nasal process is long, its orbital surface is large, and its tuberosity well marked. In the adult the vertical diameter is the greater owing to the development of the alveolar process and the increase in size of the antrum. In old age the bone approaches again the character of the infantile condition: its height is diminished and after the loss of the teeth, the alveolar process is absorbed, and the lower part of the bone contracted and diminished in thickness.

According to Gray, the lower jaw is developed principally from membrane and partly from cartilage. The process of ossification commences early—earlier than in any other bone except the clavicle. The greater part of the bone is formed from a center of ossification (dentary), which appears between the fifth and sixth week in the membrane on the outer surface of Meckel's cartilage. A second center (splenial) appears in the membrane on the inner surface of the cartilage, and from this center the inner wall of the sockets of the teeth is formed; this terminates above in the lingula. The anterior extremity of Meckel's cartilage becomes ossified, forming the body of the bone on each side of the symphysis. Two supplemental patches of cartilage appear at the condyle and at the angle, in each of which a center of ossification for these

parts appears; the coronoid process is also ossified from a separate center. At birth the bone consists of two halves, united by a fibrous symphysis, in which ossification takes place during the first year.

Further anatomic facts and details will be found in their appropriate places throughout the subsequent parts of this communication.

ODONTOGENOUS CONSIDERATIONS

Osteomyelitis of the upper and lower jaws is intimately associated with the subject of caries of the teeth, of tooth infection and of certain traumatic conditions of the teeth, and knowledge of the related odon-

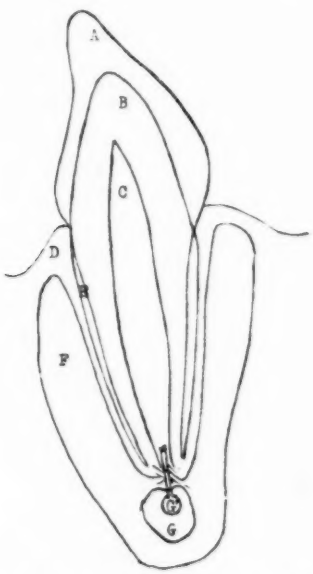

Fig. 1.—Structure of a typical tooth. *A* indicates the enamel; *B*, the dentin; *C*, the pulp and pulp cavity; *D*, the dental periosteum; *E*, the cement; *F*, the bone; *G*, the canal in the bone carrying the nutrient artery, and *G'*, the nutrient artery with an apical branch. (After Gray's Anatomy.)

togenous conditions is necessary for a proper understanding of the subject of osteomyelitis of the jaws.

The surgical anatomy of a typical tooth, as given in Gray's Anatomy, is as follows:

> A longitudinal section of a tooth will show the presence of a central cavity corresponding in a general way to the crown of the tooth. Processes of the main chamber pass from its body, one down into each root, each one opening at the apex by a minute orifice, the apical foramen. This cavity is known as the pulp chamber; the minute canals, the pulp canals. The cavity contains a soft, vascular and sensitive organ called the dental pulp. It is made up of myxomatous tissues and contains

numerous blood vessels and nerves, which enter by way of the apical foramina. It does not possess lymphatics. The periphery of the pulp is bounded by a layer of cells arranged like columnar epithelium, each cell sending one or more branched process through the basic substance of the dentin. These are the dentin-forming cells, the odontoblasts of Waldeyer. The blood vessels break up into innumerable capillary loops, which lie beneath the layer of odontoblasts. The nerve fibrils break up into numberless nonmedullary filaments, which spread out beneath the odontoblasts, and probably send terminal filaments to the extreme periphery of the pulp outside the odontoblasts.

The matrix cells and their processes are irregularly arranged in the body of the pulp, but in the canal portion the fibrillae are in the direction of the axis of the root.

Section of the tooth will exhibit three hard tissues in a tooth: one forming the greater mass of the tooth; hence its name dentin (the ivory); a layer that covers the exposed part of the dentin in the crown of the tooth, the enamel, and a thin layer, which is disposed on the surface of the fang, the cement or crusta petrosa; the cementum and enamel are thinnest at the neck and thickest on their distal portions.

The ivory, or dentin, forms the principal mass of a tooth; in its central part is the cavity enclosing the pulp. It is a modification of osseous tissue, from which it differs, however, in structure. On microscopic examination it is seen to consist of a number of minute wavy and branching tubes having distinct parietes. They are called the dentinal tubuli, and are embedded in a dense homogeneous substance, the intertubular tissue.

The enamel is the hardest and most compact part of a tooth, and forms a thin crust over the exposed part of the crown, as far as the commencement of the root. It is thickest on the grinding surface of the crown until worn away by attrition, and becomes thinner toward the neck. It consists of a congeries of minute hexagonal rods, columns, or prisms. They lie parallel with one another, resting by one extremity upon the dentin, which presents a number of minute depressions for their reception, and forming the free surface of the crown by the other extremity. . . . Numerous minute interstices intervene between the enamel fibers near their dentinal surface. It is noted in rare cases that the dentinal fibers penetrate a certain distance between the rods of the enamel. No nutritive canals exist in the enamel.

The cortical substance or cementum (crusta petrosa) is disposed as a thin layer on the roots of the teeth, from the termination of the enamel as far as the apex of the root, where it is usually very thick. In structure and chemical composition it resembles bone. It contains, sparingly, the lacunae and canaliculi which characterize true bone; the lacunae placed near the surface receive the canaliculi radiating from the side of the lacunae toward the periodontal membrane, dental periosteum; and those more deeply placed join with adjacent dentinal tubuli. In the thicker portions of the crusta petrosa, the lamellae and Haversian canals peculiar to bone are also occasionally found.

Odontogenous conditions fall into the following groups:

Superficial Caries of the Teeth.—Caries of the teeth begins in the nooks and crannies furnished by the irregularities of the crowns (i. e., the exposed portions) of the teeth. Particles of food gather there; ever present organisms—molds, fungi and streptococci of various strains—find a good haven for growth; the superficial enamel and the underlying dentin soften and gradually become eroded by attrition; a superficial cavity results. Pain is present only when the nerve endings are exposed.

As long as the pulp cavity is not entered, the integrity of the tooth is not diminished. No involvement of the jaw bone proper ever occurs with this variety of tooth condition.

Involvement of the Pulp Cavity and Root Canal.—The pathology of the dental pulp has been most completely studied by Wedl, Slater and Black, and nearly all of the knowledge now possessed on this subject has come as a result of their researches. The available knowledge indicates that there are two distinctive varieties:

1. Bacterial infection is often a source of acute hyperemia of the pulp. This is commonly caused by the invasion of the pulp chamber by the disintegrating processes of caries originating as described in the immediately preceding section. It, however, not infrequently occurs in those cases in which the pulp has not been exposed, but is still covered with a layer of decalcified and softened dentin (pseudo-exposure), the tubuli of which are filled with saprophytic and pyogenic organisms that readily penetrate to the pulp and establish irritation, inflammation, suppuration and devitalization. A thin layer of sound dentin is a positive external protection against the infection of the pulp with the pyogenic organisms.

When secondary involvement of the capillary vascular loops in the pulp cavity takes place, a much more heightened process results during the course of which the tooth structure disintegrates much more quickly. Periapical abscess formation frequently forms a part of the picture. Usually a cystic cavity results involving more than one apical area.

In a general way, superficial caries of the teeth is followed by extension of the process into the root canal and corresponds in its mechanism to direct infection of bone tissue in general following some form of trauma, as I have described in previous communications. Naturally, in exposed structures such as the teeth, trauma need be of a relatively minimal kind such as would ordinarily accompany the grinding of one tooth on another in the mastication of food. A severer trauma accompanies the biting of hard food material (the cracking of nuts), and frequently results in the breaking away of segments of the crown of the teeth. The further progression of the infection along paths produced by an eroding process parallels the further progression of an osteomyelitis of any bone under similar conditions.

2. Suppurative conditions can establish themselves in the pulp cavity and root canal without direct external infection. The presence of pyogenic organisms in the blood current, which may have gained an entrance through some abrasion of the skin or mucous membrane, or through a wound or preexisting abscess, according to Marshall, has long been recognized. These are capable, when they become arrested in a blood vessel, of rapidly propagating and of establishing suppurative

conditions. This explains the presence of abscesses of the pulp that are occasionally found in apparently perfectly sound teeth. Such dormant abscesses may not present any acute symptoms until they are opened, when, if the utmost aseptic precautions are not observed, they sometimes undergo most violent exacerbations of the inflammatory processes, which may terminate in the loss of the tooth and in extreme cases in establishing a fatal general blood infection.

The pathologic picture described in the previous paragraph corresponds accurately with the conception of the origin and pathogenesis of acute osteomyelitis of the bones of the skeleton that I have described and discussed in previous communications. Such infection of the teeth is indeed a metastatic infection.

The further development of these odontogenous conditions leads one into the subject of dento-alveolar abscess. It is found that all cases of dental infection can be grouped somewhere along this biologic development. The discussion of the subject of dento-alveolar abscess follows presently.

Pyorrhea Alveolaris.—Pyorrhea alveolaris seems to be an essentially different condition. A wide difference of opinion exists in reference to the etiology of this disease. Marshall has found, after a careful review of the literature, that the opinions can all be grouped under four heads:

1. That the disease originates in some constitutional state or dyscrasia.

2. That the disease is caused entirely by local irritation and environment.

3. That the disease is due to the infection of the tissues with micro-organisms.

4. That the disease is induced by deficient exercise of the teeth, gums and alveolar process.

Pyorrhea alveolaris primarily affects the pericementum, manifesting itself in a suppurative inflammation, sometimes acute in form, but generally of a chronic type; secondarily, the inflammatory process involves the walls of the alveolus and the gum. The gum retracts from the side of the tooth; the potential space between the root and the tooth socket becomes an actual interval as the infective and irritative process spreads downward into the socket; coincidentally, the tooth loosens in the socket and the blood supply of the tooth becomes impaired; finally, the blood supply is entirely destroyed, and a "dead" tooth results. The process is accompanied by a discharge of pus from the alveolus, and by a gradual disintegration of the alveolar process (caries); finally, the tooth loses its alveolar and gingival connection and falls out.

On the loss of the tooth, the inflammatory symptoms immediately subside, a circumstance that, according to Marshall, lends great weight to

the theory that the local manifestations of the disease are primarily associated with the dental tissues, and not with the gingivae or the alveolar processes. Witzel and others have maintained, however, that the disease is primarily located in the alveolar border, and that the gum and pericementum are involved as a secondary feature of the disease.

Fracture Cases.—Quite commonly with fracture and other injury of the jaws fractures also occur in the teeth. Usually the crown is broken away, and the root remains embedded in its socket. If allowed to remain, the root dies and infection takes place.

Dento-Alveolar Abscess.—An important item in the development of osteomyelitic foci of either of the jaws is the suppuration that occurs. In this regard all odontogenous considerations are of maximum importance. Suppuration about the teeth arising from purely dental origins is a common occurrence. The following are the important facts to be remembered from the dental point of view in considering the subject of osteomyelitis of the jaws.

In dental practice the term dento-alveolar abscess includes any accumulation of pus within a dental alveolus, or associated therewith. An acute and a chronic form of dento-alveolar abscess are described. In the acute form the symptoms are often severe, with marked local and general constitutional manifestations. Extensive necrosis of the jaw bone proper and sloughing and gangrene of the soft tissues are frequent complications, and cases are on record in which a general blood infection ensued with an eventful fatality.

Bacillus pulpae-pyogenes of Miller is, according to Marshall, generally thought to be the organism responsible for the establishment of an acute dento-alveolar abscess. It is found in decomposing and gangrenous pulps and in putrescent root canals. It is exceedingly virulent. White mice, when inoculated with it by the peritoneal route, die in from eighteen to twenty hours.

A chronic dento-alveolar abscess may be the sequel of an acute abscess that has established a fistula. A slowly developing chronic abscess also forms in the absence of any fistula formation; these are the so-called blind abscesses. These conditions, if untreated, may persist for months or years without causing any alarming objective symptoms. When a fistula exists there is, generally, a constant discharge of pus into the mouth. In both varieties of abscess the predominant micro-organism present is usually Streptococcus viridans. This is the organism that, according to Billings, Rosenow, Hartzell and others, seems to be the chief factor in the production of so many of the diseases that are now classified under the generic term of "focal infection."

In the chronic form of abscess the symptoms are usually much milder than in the acute variety, and there may even be a relative absence of

symptoms as far as the local region is concerned. Rarely exacerbations of infection occur with secondary involvement and necrosis of bone and with the local and general manifestations of a local or general infection exactly as in the acute variety.

Most of the dento-alveolar abscesses either belong to the variety commonly called periapical abscess or result as a further development of a periapical abscess. Periapical abscess is an accumulation of pus about the apex of the root of a tooth and results in the following ways:

(*a*) In one variety, a periapical abscess results from the mechanism by which involvement of the pulp cavity and root canal occurs following an initial superficial caries, as described in the previous sections.

(*b*) A periapical abscess forms after trauma that results in fracture of a tooth, especially when the line of fracture passes through the root; also after an operative trauma during which fragments of instruments have been broken off and left in the pulp or root canals. A nonvital tooth results and leads to the formation of the periapical abscess.

(*c*) A periapical abscess is frequently found in the alveoli of vital teeth, as, for instance, in pyorrhea alveolaris and in inflammatory conditions arising from various forms of irritation and traumatisms of the pericementum.

(*d*) In the absence of other demonstrable pathologic changes (traumatic or otherwise) in the given tooth, a periapical abscess represents, in my opinion, a metastatic infection following a pathogenesis similar to that in ordinary types of osteomyelitis of other bones. The establishment of the given point of fixation depends on minor traumas incident to the grinding and mastication of food, and the inflammatory process centers in the vascular channels present in the depths of the socket from which the nutrient artery of the tooth is derived. A relatively circumscribed lesion results marked by erosion of the tip of the root and of the adjacent walls of the tooth socket, and by the formation of a minute abscess cavity lined by a granulation membrane. The bacteriologic content of the abscess is the streptococcus.

Another form of dento-alveolar abscess is one that has no external sinus for the discharge of the pus. These cases have been for this reason designated as blind abscesses. The term is, however, hardly a correct one, for the pus discharges through the pulp canal, which becomes its sinus, and it is therefore not a blind abscess. These abscesses are usually small, and, as a rule, are not very painful; in fact, all of the acute symptoms are greatly modified by reason of the ready exit of the pus from the beginning of the suppurative process. A blind periapical abscess of this variety has a good many similarities to the chronic type of bone abscess found in the long bones, which was first described by Brodie.

CLINICAL GROUPING OF CASES OF OSTEOMYELITIS OF THE JAW

Cases With and Without Odontogenous Factors.—A number of clinical groups and subgroups can be distinguished as the cases of osteomyelitis of the jaws present themselves. Theoretically, the distinctions are easily made; in actual practice, however, the groups are not always so easily definable, and the proper integration of an individual case is frequently a matter of difficulty. In each of these groups one commonly finds: (1) Cases in which odontogenous factors can be definitely excluded, and (2) those in which odontogenous factors play a distinct rôle and must be included.

This phase of the study will properly be appropriately included as it applies in the discussion of each of the previous groups. In actual practice, the classification of any given case is made difficult because of any odontogenous association. According to the mechanism involved, one can distinguish:

Primary cases.
Extension cases.
Hematogenous cases.

Primary Cases: Osteomyelitis of the jaws, in contradistinction to osteomyelitis of the other bones of the skeleton, is quite frequently a primary process and does not depend on hematogenous infection. Direct infection of the bone tissue occurs only through the intermediation of some trauma. In accordance with the manner of application of the trauma, three groups can be distinguished:

Civil injuries—falls, blows, etc.
Gunshot wounds, including those in civil life as well as in military practice.
Osteomyelitis following operative manipulations, wiring of fractures, excision of tumors, cysts, etc.

Gunshot wounds form a class by themselves and will not be discussed in this communication. The essential difference between gunshot wounds in civil life and during a military emergency lies in the depleted and exhausted condition of troops on the battle-line and in the enormous increase in environmental contamination (usually of a fecal nature) incident to active warfare in the field.

Osteomyelitis following operative manipulation results from an exposure of bone tissue, or from the opening of vascular channels leading into the bone tissue, or as a result of operatively produced or postoperative spontaneous frank fractures that result from the removal and consequent weakening of the bone structure. This variety follows the course usually seen in the ordinary civil form of injury to the jaws followed by infection of the bone tissue.

Odontogenous factors enter in primary cases of osteomyelitis of the jaws when the effects of the primary trauma include the breaking away

of portions of the crowns of the teeth, or when the line of fracture of the jaw passes simultaneously through the roots or sockets of the teeth. A devitalization of the given tooth or teeth follows immediately, and dental surgeons have learned to extract such teeth immediately in order to obviate any subsequent trouble, at least as far as the dental factor is concerned. This precautionary procedure immediately removes this element of the discussion.

Infection of the bone following the ordinary form of trauma sustained in civil life occurs because of the presence of a compound fracture of the jaw. The line of communication with the exterior, in the vast majority of the cases, leads into the interior of the mouth through a rent in the mucous membrane. Contamination and infection occur immediately, and the degree of the contamination and the resulting infection seems uncontrollable by any means at command, as it is impossible (1) to cleanse and to perform débridement of the wound properly, (2) to close the wound in the mucous membrane adequately and (3) to prevent the continuous introduction of additional infection.

The essential pathologic changes include the introduction of infection into the opened vascular channels (thrombophlebitis), beginning in the plane, and on either side, of the line of fracture. The amount of pathologic change and its intensity depend (1) on the kind and virulence of the infecting organism and of its opposing antibody formation, (2) on the amount of disturbance of blood circulation and (3) on the character and degree of the consequent deprivation of food supply from the bone cells. The last item determines the amount of bone necrosis.

There is a tremendous variation in the amount of necrosis that follows. In those fortunate cases in which the anatomic position of the fragments is such as to encourage free drainage and in which, also, secondary thrombosis and blockage of the blood stream do not reach into a blood vessel of sufficient size, the number of bone cells that die and the amount of bone that becomes devitalized are absolutely or relatively small or entirely absent, and the wound heals by granulation with minimal, or without any, sequestration. When the opposite condition prevails and a major trunk becomes thrombosed, relatively large amounts of bone sequestrate. Between the two extremes, naturally, the latitude of variation is infinite. In my own experience, I have met with examples of all kinds, from those in which no bone at all is sequestrated to those in which sequestrums measuring several inches in their largest diameters have subsequently been discharged from the sinuses, or have been removed at operation. Usually, however, the amount of bone tissue that sequestrates is relatively small and represents a marginal necrosis at the line of fracture. Suppuration either does not occur or is of minimal extent. In all respects the pathologic picture is similar to that in cases of osteomyelitis of the long bones complicating a compound

fracture in which the focus develops in the vascular network, as described elsewhere. Depending on the size and importance of the vascular channel that is thrombosed and on the abundance of the collateral circulation, little or no bone necroses or larger segments become involved and finally sequestrate.

Extension Cases: Most of the cases of osteomyelitis of the jaws should be classified as extension cases. By that I mean that the osseous lesion is due to the spontaneous extension of the infection along vascular channels into the jaw bones from an area of infection in close proximity with the bone. The subgroups are as follows:

1. Extension from a lesion in the attached soft parts.
2. Extension from a lesion in the gum.
3. Extension of odontogenous origin.
4. Extension after operative manipulation.
   (*a*) After dental operations.
   (*b*) After surgical operations on the jaws.
   (*c*) After dental manipulations, including the use of carbolic acid or of arsenic.

1. This group includes cases in which osteomyelitis of the jaw—and here it is practically invariably the lower jaw—has resulted from an extension of an inflammatory focus in the soft parts clothing the bone. The number of cases in this group is comparatively and actually very small.

A few cases have been reported in which staphylococcus infections of the chin have progressed sufficiently deeply to involve the underlying lower jaw. This has been the point of view of most of the observers. While Herrath expressed the belief that ordinarily this is a hematogenous infection, he, nevertheless, acknowledged that the extension mechanism is extremely possible in diabetic and other similar subjects.

2. Hauenstein quoted Williger, who reported a case of chronic osteomyelitis of the lower jaw that resulted from an ulcer of the gum in the region of the molar teeth.

The extension mechanism for osteomyelitis of the jaw in cases of this kind is dependent on the character of the vascular supply. The characteristics to be described are applicable to the lower jaw almost entirely and explain the reason why extension cases are almost invariably in association with the lower jaw. The blood supply of the lower jaw, as indicated elsewhere, consists of the nutrient (inferior dental) artery and of the periosteal circulation derived from contiguous muscular and other arterial trunks. The latter supply is very abundant, and individual vessels must necessarily be implicated from time to time when inflammatory lesions in the soft parts clothing the bone are appropriately placed. That such vessels will undergo thrombosis is

obviously to be expected, and an extension of the infection along the thrombosed vessels follows as a matter of course. Should such an infected thrombotic process spread inward sufficiently far to enter within the confines of the jaw, an osteomyelitis results, and any compromisation of blood supply is evidenced by a corresponding necrosis and sequestration.

I remember seeing this sequence of events on one occasion in the upper jaw:

> A man approximately 60 years of age came to the hospital with a gangrenous process involving the gum covering the posterior extremity of the upper alveolar process. When the slough began to separate, it was found that bare necrotic bone underlay it. After several weeks, a large sequestrum separated spontaneously. There was no other definite etiology to be determined for the bone necrosis.

I explain this pathologic picture on the following anatomic and pathologic grounds: The gangrenous process in the gum, because of its position, involved the gingival branch of the posterior dental artery (hence the gangrenous character of the process). Thrombosis of this vessel occurred as a matter of course. Extension of the thrombotic process occurred in a retrograde manner into the trunk of the posterior dental artery. Necrosis of that portion of the alveolar process followed as a result of the deprivation of the blood supply, and resulted in the discarded sequestrum.

3. Cases of odontogenous origin are, of course, the commonest examples of the extension group. Nevertheless, spontaneous extension of the infection from a diseased tooth into the bone tissue of the jaw is comparatively uncommon. Anatomically, this would indicate that the pathologic process had extended in a retrograde fashion by a progression of the thrombosis into one or more of the larger branches, or into the main trunk of the dental artery (superior or inferior, depending on which jaw was involved), and had led to compromisation of the blood supply and consequent necrosis and sequestration.

4. The cases that follow some operative (usually dental) trauma form the largest number of the cases in the extension group seen in ordinary practice. The dental manipulation or operation may be performed in cases in any of the groups considered in the section devoted to odontogenous considerations of the subject, and the operative procedure varies from the cleaning out and repair by filling of the cavities, to tooth extraction and possibly other manipulations. The usual clinical history includes the general and local symptoms associated with focal infection of one kind or another, or a frank toothache, a visit to the dentist during which an extraction is usually done and an almost immediate onset of pain in, and a swelling of, the jaw, accompanied by chill, fever and other constitutional manifestations of a bacterial infec-

tion of more or less virulence. The history frequently includes one or several additional operations during which additional incisions were made along the gums, or externally, with little or, more usually, no relief; a characteristic manifestation is an exaggeration of the objective symptoms each time these additional incisions are made. Finally, roentgen studies show the presence of sequestrating bone, and the diagnosis is established, if not suspected before that time.

The preexisting lesion in and from which the exacerbation and spreading of the infection originate is a variety of dental infection; frequently some variety of dento-alveolar abscess is present, usually the simple periapical abscess. Such cases are undoubtedly due to the mechanical spreading of infection along newly opened planes and their transmission into healthy vascular channels of the cortex and interior of the jaw bones. Secondary vascular thrombosis is always present, and the extent of this determines the amount of devitalization and the extent of consequent necrosis of bone.

Another extension type of necrosis of the jaw of odontogenous origin, which used to be seen many years ago, is that which followed the injection of carbolic acid or the use of arsenic. This practice has been wisely given up by practically all dentists.

I have the records of one case in which the injection was done for the relief of pain. Extreme pain and swelling followed immediately, and after a very stormy time in which necrosis of almost the entire alveolar process of the upper jaw resulted, a sequestrum was extracted by operation, and healing ensued in a very slow manner.

Blair and Brown reported the following case:

In a woman, aged 32, some arsenic was left in a tooth for two weeks. There was a local abscess; many teeth became loose, and there was widespread necrosis of the jaw. Several teeth extractions and sequestrotomies were necessary.

Hematogenous Cases: The mechanism of the pathogenesis and pathology of hematogenous osteomyelitis in general has been discussed extensively on a number of previous occasions, and an extensive discussion of this subject will not be repeated here. Suffice it to say in résumé:

Acute hematogenous osteomyelitis is a metastatic lesion that develops during the course of bacteremia, the latter resulting from an acute bacterial lesion on a surface of the body that forms the portal of entry for the infection. In this conception, a surface of the body includes not only the skin, but also the entire mucous membrane of the alimentary tract, the genito-urinary tract, etc. The common surface lesions include not only furuncles, carbuncles, etc., on the skin, but also easily demonstrable lesions in the tonsils, and in other lymphadenoid collections lying in the mucous membrane of the pharynx, as well as less demonstrable lesions, such as those in Peyer's patches.

The fundamental cause of the spreading of the original lesion in the form of metastatic or subsidiary lesions is an infected thrombus lying in the original area of infection, and communicating at some point with the freely circulating blood. The organisms growing on the surfaces of the thrombus are discharged, or pieces of the thrombus itself break off and are discharged into the circulation, and, becoming lodged for various reasons in the vascular network of various parts of the body, give rise to secondary lesions. Bone tissue, because of its peculiarities in vascular structure, seems particularly prone to the blocking of these thrombi-emboli, and the susceptibility to this condition is particularly increased during the period of growth when the individual bones contain well marked hyperemic areas at the junction of the diaphysis and epiphysis, around centers of ossification, etc.

The various accessory causes, such as trauma, that determine the localization of a secondary focus of infection—fixation point—in a given bone are associated with accidents in the local circulation which facilitate blocking of any bacterial thrombus-embolus.

Mengel described a case of osteomyelitis of the upper jaw with secondary empyema of the antrum, which followed trauma to the root of the nose. Lichtwitz has also noted osteomyelitis following trauma to the side of the face. In this instance, the antrum was not affected.

The essential nature of the pathologic process that develops at the fixation point is a thrombo-arteritis or thrombophlebitis, and the process in the vertebrae is exactly similar to that in other bones in which a dominating position is assumed by the secondary vascular thromboses that must necessarily occur in such a pathologic lesion. The all-important secondary effects that these thromboses produce are disturbances of essential nutrition, which lead to the death of certain bone cells, and the consequent necrosis of certain areas of bone tissue.

Proof that a hematogenous origin for an osteomyelitic lesion of the jaw occurs is furnished by the relatively abundant occurrence of cases of osteomyelitis during the course of infectious disease, especially when specific organisms such as typhoid or influenza bacilli play the etiologic rôle, and by the occurrence of chronic bone abscesses in the jaw. Cases also occur ordinarily when the character of the bacteriology, i. e., the finding of Staphylococcus aureus, makes it strongly suggestive that the lesion in the jaw is of blood borne origin.

According to Marshall, hematogenous infection of the teeth also occurs; a differentiation as far as the odontogenous considerations are concerned is attempted by Marshall on the following basis:

> When the symptoms are first noted immediately after the treatment of a quiescent nonvital tooth this rather suggests a preexisting periapical streptococcus infection which may have been present for years. When such an infection involves a tooth with intact walls it must be considered as being of blood-borne origin.

In actual practice, hematogenous cases are seen by the dentist as the periapical variety of dento-alveolar abscess easily distinguishable on the criteria presented by Marshall. The surgeon seldom sees hematogenous cases of osteomyelitis of the jaws with such clearcut etiology. Usually by the time the patient comes for treatment the lesion is so extensive that it apparently implicates the tooth and the jaw, and it becomes impossible to evaluate cause and effect except on certain circumstantial evidence, such as (1) the presence of a suggestive or specific bacteriology, (2) the association with an acute infectious disease or (3) certain clearcut forms of pathology as, for instance, a bone abscess buried deep in the bone tissue and isolated from the adjacent teeth. In most instances the dental pathology seems to dominate the picture, and it is usually assumed that the latter is the cause of the entire lesion, whereas,

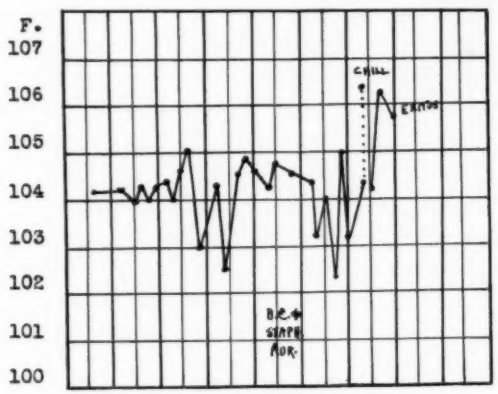

Fig. 2.—Temperature chart.

as a matter of fact, it is possible for a hematogenous infection to form points of fixation (1) either in the teeth or in the jaw, with subsequent extension of the infection from either one to the other; (2) in both the teeth and the jaw simultaneously, or (3) in both the teeth and the jaw at subsequent times with coalescence of the foci into a seemingly single lesion. The following case is illustrative.

An 8 year old boy was admitted to the hospital with an alveolar abscess of the left mandible following the extraction of a tooth performed several days before admission. The temperature on admission was 104 F., and the patient appeared very toxic. There was marked swelling over the left side of the jaw, but no point of fluctuation. As shown in figure 2, the temperature fluctuated between 103 and 105 F. In spite of apparent local improvement, the general condition became worse. Ten days later, the patient complained of pain in the right elbow, and a metastatic focus was found in the lower end of the humerus and was opened. Again there was improvement, but again the patient became toxic and went into a state of stupor and coma. Cultivation of the blood showed Staphylococcus aureus. The patient died two days later.

The clinical picture resembled accurately that seen in cases of sepsis associated with the ordinary form of acute osteomyelitis.

Hematogenous infection of the tissue of the jaw occurs in association with the following conditions:

1. Osteomyelitis following the ordinary local form of infection.
2. Osteomyelitis following or coincident with infectious diseases.
3. Osteomyelitis in nurslings and infants.
4. Osteomyelitis in adults with unerupted teeth.
5. Chronic bone abscess of the jaw.

1. Osteomyelitis following the ordinary local form of infection. Cases of osteomyelitis of the jaws following foci of infection, such as furuncles, etc., as with other bones of the skeleton, are relatively and actually rare. Perthes classified the commonest infecting organisms as the staphylococci.

2. Osteomyelitis following or coincident with infectious diseases. The mechanism and pathogenesis of cases of osteomyelitis of the jaws that arise in the course of an acute infectious disease are similar to those that occur as hematogenous infections of bone elsewhere and under ordinary conditions. The position of the jaws in the mouth and the necessity for cleansing and other manipulations of the mouth make these bones particularly prone to traumatisms of all kinds and to carious conditions around the teeth. While in possibly a very few cases the osteomyelitis of the jaw may conceivably be a direct extension from an ulcerative stomatitis or other generally similar condition, the traumatisms that are demonstrable are more probably agents in determining the localizations than primary portals of entry for the infection. The assumption seems all the more probable because specific bacteria, for example, typhoid or influenza bacilli, etc., are found in the bone.

The important infectious diseases that can be complicated by osteomyelitis of the jaws include typhoid fever, influenza, measles and scarlet fever. There are such reports in the literature by Mantell, Schmiegelow, Heath, Patissier, Gagliardi, Salter, Layton, Albanese and others. Less often it occurs after chickenpox, smallpox, diphtheria and typhus fever. The type in the exanthematic cases may be bilateral, as in a case described by Cadenat and Cola.

According to Perthes, cases are most common in association with typhoid fever and influenza. Cases of typhoid fever have been reported by Perthes, Albanese, Burkett and others.

(*a*) According to Salter and others, cases of osteomyelitis of the jaws are most common after scarlet fever. In the official reports of the Metropolitan Asylums Board (which controls all the fever hospitals of London) for 1897, Mantell described 19 cases of necrosis of the

jaw in a series of 12,230 cases of scarlet fever. In 16 of these there was a common factor determining the necrosis, viz., mechanical injury. The throat and mouth were, of necessity, frequently cleansed, and food was given at frequent intervals; the patients actively resisted this treatment. The necrosis began in the height of the acute stage, close to the symphysis of the lower jaw. Seven of the 16 patients died. In only 3 was the upper jaw involved, and of these 2 recovered. In those days syringing the throat was a common method of treatment, and to do this the gag was frequently needed in a recalcitrant child. Of the 3 other cases, 1 was a case of general ulcerative stomatitis occurring in the fourth week and ending in death. The 2 others were associated with alveolar abscesses around a carious tooth.

(*b*) Two cases were reported by Layton in 1928. In his report he referred to the fact that cases had rarely been seen after smallpox. In some of these cases necrosis of the jaw resulted in communications with the antrum; a pansinusitis was also present.

The osteomyelitis of smallpox divides itself into two distinct groups. The first, a rather infrequent complication, is the suppurative type, which occurs as a result of secondary infection. The second is due to the variola itself, occurs during the course of the disease and has all the histologic characteristics of the typical smallpox lesion. This type of osteomyelitis is nonsuppurative and resembles closely the lesions found in orchitis variolosa. Chiari, in 1892, described osteomyelitis variolosa in detail. In a large number of necropsies on patients with smallpox, he found necrotic foci widely distributed through the bone marrow of the long bones, and, in a few cases, in the sternum and vertebrae. The lesions were found as early as two days and as late as two months after the appearance of the eruption, without any evidence of suppuration, even in the late cases. Although he found this condition in 86 per cent of the cases he examined, there are very few clinical case reports.

In 1910 and 1913, Musgrave and Sison reported 20 cases of marked bone deformities in adults from whom they obtained a history of smallpox in childhood. The fact that the bone disturbance began to manifest itself first during the course of the attack of variola, together with the work of Chiari, led them to believe that this was the etiologic factor. From the character of the deformity—a shortening of the long bones with no disturbance in circumferential growth—they inferred that the site of the disease was either in the epiphysis or in the area of growth. Since then there have been several other cases reported.

(*c*) A case of osteomyelitis of the jaw with complete necrosis was reported by Patissier to have occurred in a soldier during the course of typhus fever. This seems to be extremely rare.

3. Osteomyelitis in nurslings and infants.[1] A considerable literature has grown up around the cases of osteomyelitis of the upper and lower jaws that is found to occur in nurslings and infants. The first case reported in the British literature was by Douglas, in 1898; in the American literature, by Posey, in 1912. Since then numerous communications have appeared in the literature of the various continental and American countries.

Practically all writers agree that the disease must be of bacterial origin, but there is considerable controversy as to whether or not it is a primary lesion of the jaw bone, a minority believing that it is a hematogenous infection of the jaw. The majority believe that it is a primary infection of the bone, the portal of entry being somewhere along the gum, in the teeth buds, the nose or the antrum, aided and localized by various forms of trauma during childbirth or thereafter.

The available sources for the infecting organisms are (1) the vaginal canal of the mother, (2) the fingers of the accoucheur or the nurse, (3) the nipples and breasts of the mother and (4) the fingers or apparatus employed in cleansing the baby's mouth.

Pathologically, the brunt of the infection centers in the entire jaw bone, much more often in the upper than in the lower. Usually, the entire bone seems to be involved almost at once, and the process exhibits itself either simultaneously or in quick succession on the palatal, nasal and orbital aspects of the bone in the form of abscesses; the teeth are quickly exfoliated, a discharge appears from the nose, and an orbital abscess forms. Necrosis and sequestration of the jaw bone follow.

In explaining this pathologic picture, the various writers have attempted to find origins for this extensive process in a primary process in the nose, in the unerupted teeth buds (Kleming, in the Koerner Clinic) or in the antrum of Highmore (Paunz, of Budapest).

My own impression and belief are that osteomyelitis of this type occurring in nurslings and infants is in no way different from the hematogenous form of osteomyelitis in general occurring in other parts of the body, and that the occurrence of the lesion in such young subjects is associated with the physical conditions of childbirth and the environmental conditions immediately following. The localization in the jaws is, as is held by almost everybody, due to various forms of minor or major injury received during childbirth or to various forms of trauma received thereafter associated with the care of the child, especially with cleansing of the mouth. The predilection of the upper jaw is due to its larger size and its more rigid construction and attachment in the skull, which favor the more frequent reception of traumatisms.

1. An extensive discussion of this group of cases of acute osteomyelitis of the jaw in nurslings will be made in another communication.

The presence of unerupted teeth and teeth germs or buds determines areas of more marked vascularity, which help to determine points of fixation for the metastatic infection. The traumas described as occurring on the alveolar border or elsewhere, which are taken to be the primary points of entry for the infection, should not be assumed to make pathways directly to the bone; these traumas favor the formation of a locus minoris resistentiae. The transmission into the substance of the jaws is made possible by way of the blood stream and not by simple extension by contiguity.

The actual pathogenesis and pathology are exactly similar to those in other cases of hematogenous osteomyelitis. The point of fixation in the vascular channels of either of the jaws develops into a thrombophlebitis. The occlusion of the vascular channels results in the usual deprivation of blood supply and nourishment, and the amount, degree and character of the resultant necrosis are in direct proportion to the number, size or importance of the vascular channels occluded and the amount of available collateral circulation (see section on "Bone Necrosis in Osteomyelitis of the Jaws," p. 215).

The controversy as to whether or not this form of osteomyelitis of the jaw centers and is derived from a lesion in the teeth buds, the nose or the antrum is to my mind unnecessary and fruitless, as, from the facts outlined, one can easily see that all of these manifestations are simply determined by the dominating position of the thrombophlebitis in the course of the vascular channels described. The seeming importance of any one manifestation is only superficial, and the character of the pathogenesis and pathology is, as in other forms of acute osteomyelitis, intimately related to the position of the thrombophlebitis and the resultant necrosis.

The disease presents a clearcut, definite, clinical picture, one case report being similar to the others. Usually in a healthy infant a few weeks old, unidentifiable prodromal symptoms are followed by high fever, vomiting and prostration. A swelling then appears, beginning in the cheek or the infra-orbital region, and almost always there is edema of the lower eyelid. The sclera is inflamed, a conjunctivitis is present, chemosis is sometimes noticed, and not uncommonly some exophthalmos is present. An abscess forms in the swelling. Similar swellings and abscess formations form on the palate or alveolus in the mouth, and teeth buds exfoliate through the resultant fistulas. A purulent discharge escapes from the nose, which seems to be connected with the swelling in the cheek. All of this occurs in a very few days. The temperature continues irregularly, convulsions are frequent, and there are marked anorexia and difficulty in nursing. The outcome is healing with or without the persistence of sinuses, the development of metastatic

purulent foci or the infant dies as a result of the virulence of the infection, either before or after secondary foci appear.

The mortality is large, varying from 25 to 50 per cent in the various series of cases reported in the literature. The final result, when the infant lives, is a considerable deformity of the face and palate, with loss of the teeth, both temporary and permanent, on the side involved.

The differential diagnosis is to be made between this form of osteomyelitis and the following conditions:

1. Ophthalmia neonatorum. This is usually a bilateral lesion, and gonococci can be demonstrated.
2. Erysipelas.
3. Dacryocystitis.
4. Syphilis.
5. Tuberculosis.

Careful examinations usually clear up the diagnosis.

4. Osteomyelitis in adults with unerupted teeth. I have seen patients with osteomyelitis of the jaw—usually the lower jaw—with typical sequestration of portions of the alveolar processes or of the bodies of the bone in whom roentgen studies demonstrated an unerupted tooth buried deeply in the bone tissue. The initial stages of the local condition are not accompanied by any apparent tooth infection, although, invariably, such an assumption is made, as the patient interprets the pain as "toothache." Indeed, in one of my cases the erupted teeth at the locality of the process were missing. No wound or other traumatic condition of the gum is present. The clinical course includes the usual manifestations up to and including the sequestration, the separation and the exfoliation of the necrotic portions of the jaw. Subsequent closure of the wound or fistula does not, however, occur until the unerupted tooth is removed at operation.

I interpret the sequence of events as follows: A hematogenous infection takes place in the bone tissue surrounding the cavity of the unerupted tooth, the latter possibly forming the determining factor for the point of fixation; interference with the food supply of the unerupted tooth is a secondary phenomenon resulting from the compromisation of the vascular channels of that portion of the jaw bone itself involved in the inflammatory process; the unerupted tooth then acts as a foreign body and prevents the healing of the wound until it is removed.

5. Chronic bone abscess of the jaw. In 1858, Nussbaum described a bone abscess of the left side of the lower jaw in a 21 year old woman. Frankel, Herzog (1889), O. Faisst Kuhn, Weise and many others have also described similar cases. I have, personally, never encountered such a case. It is a curious fact that these reported cases have occurred

in the lower jaw. It is impossible for bone abscesses of this type to form in the interior of any bone, unless on a hematogenous basis.

It is a nice point for discussion, whether or not a hematogenous periapical abscess of the teeth should not more correctly be classified as a chronic bone abscess of the jaw. As indicated previously, the blood supply of the individual teeth is furnished by terminal arteries, branches of the corresponding dental artery, which perforate the fangs of the teeth at their apexes and penetrate the pulp cavity of the teeth (fig. 1). A thrombo-embolic process that became centered in these terminal branches would result in a small abscess immediately surrounding the vessel, which, because of the very nature of the anatomic arrangement, would be situated around the apex of the fang of the tooth; hence the name, periapical abscess. The association of this variety of dento-alveolar abscess with dental practice has apparently been determined because of the proximity of the teeth, whereas, in truth, it might more correctly be classified with diseases of the jaw.

SUPPURATION WITH OSTEOMYELITIS OF THE JAWS

Knowledge of the forms and varieties of suppuration about an osteomyelitic focus in either of the jaws is important from the point of view of surgical treatment, and in this regard a complete understanding of the odontogenous factors is necessary. It appears that when a tooth is the seat of an acute dento-alveolar abscess, there is always a considerable involvement of the bony structure at the apex of the root. The pus is at first confined to the apical space, where it is surrounded by bony walls. As the pus accumulates, a disintegration of the surrounding cancellated bone takes place, and a gradually increasing cavity is formed around the apex of the root. Such disintegration should, however, not be classified as a form of osteomyelitis of the jaw unless secondary involvement with destruction of bone cells can be demonstrated in the jaw bone proper as a result of thrombophlebitic involvement of the vascular channels in the bone.

As the external or buccal wall of the alveolar process is the thinnest, it offers the least resistance to the progress of the constantly accumulating pus; for this reason the abscess usually burrows through the external plate in its further development and points on the buccal aspect of the alveolar process opposite the apex of the root. Dento-alveolar abscesses can, however, point in the following other ways after penetrating the bony walls of the tooth socket:

1. Directly through the soft tissues. Dento-alveolar abscesses that point directly through the gum tissues are the most common, and rarely present any complications. Many of these are the common gum-boils.

2. By separating the periosteum from the bone and forming a secondary pus pocket.

3. By following the pericementum along the side of the root and discharging at the margin of the gum. These abscesses are sometimes confounded with the so-called blind abscesses, but in these cases a careful examination will reveal the fact that there is no discharge through the pulp canal. Many times this form of abscess is associated with pulpless teeth, the roots of which have been filled, but in which there is sufficient bacterial irritation to keep up a chronic discharge of pus through the sinus that has been formed by the side of the root.

4. Occasionally, pointing toward the tongue.

5. Through the floor of the nasal fossa. The relations of the roots of the incisor and cuspid teeth to the floor of the nose are such, in many instances, that appropriately placed dento-alveolar abscesses may point through the floor of the nasal fossa and produce a purulent discharge that might readily be mistaken for chronic nasal catarrh. The relations of the roots of the bicuspids and molar teeth to the floor of the antrum are such as to make it even less difficult for an abscess connected with one of these teeth to penetrate the floor of the sinus.

Clinically, as soon as the pus penetrates the bony walls of the abscess and escapes into the soft tissues, the severity of the pain is abated, but the tissues begin immediately to swell, and sometimes the swelling is very great. When the abscess is associated with the upper jaw, it not infrequently closes the eye. When located in the lower jaw, in the region of the molars, it may be so extensive as to make deglutition impossible, and greatly obstruct breathing. This condition is sometimes erroneously diagnosed as Ludwig's angina.

Acute dento-alveolar abscesses rarely heal spontaneously; there is, however, a partial filling up of the pus cavity by the growth of granulation tissue. But there is usually a sufficient amount of decomposition of tissue and growth of micro-organisms within the abscess cavity and the pulp canal to keep up the suppurative process.

Occasionally, a dento-alveolar abscess may present chronic symptoms from the very beginning of the suppurative process, as, for instance, in blind abscesses. There are often a prolonged and obstinate irritation at the apical space and a persistent accumulation of pus, which finds an exit through the pulp canal, and the toxins of which are taken up and absorbed by the blood current or the lymphatic stream. These abscesses are among the most dangerous to the general health of the patient, as they are fruitful sources of general sepsis. Teeth so affected, which do not respond to treatment after a fair trial, should be extracted.

Abscesses that have pointed through the external tissues of the face are nearly always of a chronic type, particularly those that have had

their origin in ancient traumatisms, perforation of the cementum, broken instruments within the root canal or from an impacted position of a tooth.

I think it should be assumed in cases of osteomyelitis of the jaws associated with odontogenous factors that any suppuration beyond the simplest forms should be ascribed to the associated lesion in the jaw bone. In going through the various dental contributions, it is worthy to note how frequently the suppurations described are said to be complicated by necrosis of portions of the jaw bones. Any suggestion of necrosis of the jaw should, of course, remove such suppuration from the category of dental to that of the jaw bone osteomyelitis proper, even though the shedding of a sequestrum is not always necessary to prove the involvement of bone, because these are essentially subperiosteal abscesses that are not always associated with necrotic bone.

The character and localization of any suppuration derived from an osteomyelitis of the jaws are determined by the anatomic contour of the bones, and by the attachment of muscle tendon and fascial planes. (*A*) The common locations of abscesses derived from osteomyelitis of the upper jaw are (see section on "Treatment," p. 225) as follows:

1. In the maxilla, the commonest location is in the cheek. The abscess spreads upward and outward toward the orbit and the zygoma. The subcutaneous tissues are very loosely applied to the underlying bone, and an abscess of considerable size develops.

Abscesses that gather in the cheek have a tendency to be accompanied by much necrosis of the subcutaneous tissue of the cheek. I believe that this has some relation to a thrombo-embolic lesion of the posterior alveolar gingival and buccal arteries which supplies the tissues of the cheek as well as the alveolus (fig. 3).

2. As has been described (see section on "Osteomyelitis in nurslings and infants," p. 203), abscesses develop also in relation to the nasal, palatal and orbital surfaces of the upper jaw.

(*a*) The abscesses pointing into the nose never attain a large size before they rupture spontaneously; as a matter of fact, these localizations are commonly not recognized clinically until they do rupture. Anatomically, the nasal localizations of the abscess are related to branches of the anterior dental artery and to the branches of the nasopalatine artery that supplies the nasal surface of the superior maxilla.

A case of localization of the osteomyelitic process on the nasal surface of the maxilla with secondary empyema of the antrum was reported by Menzel.

A 21 year old man sustained an injury of the root of nose. Quite soon thereafter he fell ill with pain in the region of the frontal sinus, and there seemed to be involvement of the orbit. There were high fever and other signs of a general infection. After one week a discharge of pus and blood occurred from the nose, and

the subjective symptoms disappeared. The discharge of pus continued. Bone necrosis was suspected, and at the operation it was determined that necrosis of the nasal wall of the antrum had occurred. The frontal sinus manifestations were due to involvement of the duct in the inflammatory process.

(*b*) Abscesses accumulating on the palate are derived naturally from the palate process of the maxilla and are related to lesions in the palatal vessels. They are seen most frequently in nurslings and infants. They are usually subperiosteal abscesses.

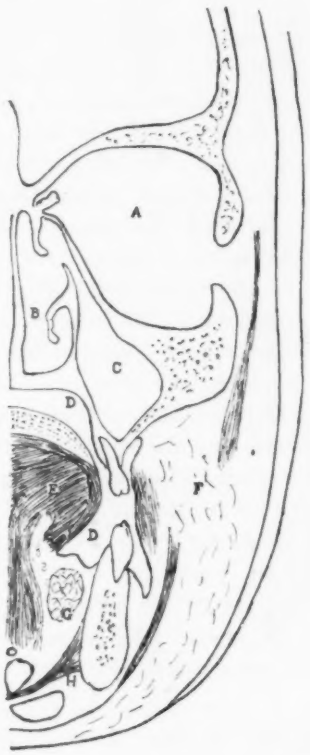

Fig. 3.—Cross-section to show the relationship of the alveolar arches and the contiguous cavities and areas. *A* indicates the orbit; *B*, the nasal cavity; *C*, the antrum; *D*, the oral cavity; *E*, the tongue; *F*, the cheek; *G*, the floor of the mouth; and *H*, the submaxillary triangle. (From the Manual of Surgical Anatomy, Medical Departments, United States Army and Navy, 1918.)

(*c*) Pus that accumulates on the orbital surface of the upper jaw forms an orbital abscess that quickly causes marked chemosis, induration and swelling of the orbital fat with protrusion of the eyeball and fixation and closure of the lids. Spontaneous rupture commonly occurs in the area contiguous to the inner canthus. In the further development of the abscess, the suppuration extends upward to the roof of the orbit.

The anatomic basis for the orbital localization of the bone lesion and its consequent suppuration is a lesion in the infra-orbital artery as it lies in the floor of the orbit (i. e., the orbital surface of the superior maxilla).

In nurslings and infants, all three of these localizations commonly occur simultaneously.

3. A group of cases occurs in which the suppuration extends into the antrum of Highmore, and an empyema of the latter cavity occurs (figs. 3 and 4).

The antrum of Highmore, or maxillary sinus, is a large pyramidal cavity in the interior of the maxillary bone. Its walls are everywhere exceedingly thin, and correspond to the orbital, facial and zygomatic surfaces of the body of the bone. Its inner wall contains a large irregular aperture, which communicates with the middle meatus of the nasal fossa. The posterior dental canals, transmitting the posterior dental vessels and nerves to the teeth, are on the posterior wall. Several conical processes, corresponding to the roots of the first and second molar teeth, project into the floor of the antrum; in some cases, the floor is perforated by the teeth in this situation. The antrum is lined by a continuation of the mucoperiosteum, which covers the surfaces of the nasal fossa and its accessory sinuses. The anatomic basis for involvement of the antrum is usually a lesion in the posterior alveolar and posterior dental arteries so placed that the necrosis of the alveolus which subsequently occurs includes the lower and outer angle of the bony wall of the antrum. The antrum becomes infected by contiguity. Commonly, the physical characteristic of such a lesion is a peculiar gangrenous infection of the upper jaw, which results in the sequestration of such a large segment of the alveolar process and body of the upper jaw that the antrum is laid wide open.

I have the records of two cases of this kind.

A man, approximately 45 years of age, who had a history of prolonged and profound indulgence in alcohol and other excesses, complained of toothache that seemed to be caused by an infected tooth. Very quickly a foul odor became apparent, and a gangrenous process developed in the surrounding tissues, which quickly acquired a line of demarcation. No definite, extraordinary, etiologic cause (poisoning by heavy metals, leukemia, etc.) was demonstrable. When the dead tissue was removed at operation, one could look into a large hole, the apex of which was the antrum of Highmore. In spite of the fact that the dead tissue was removed at the earliest possible moment, the general condition of the patient became progressively worse, and he died.

In a man, approximately 60 years of age, an infection developed around one of the lateral teeth of the upper jaw. An abscess formed. The tissues thereafter assumed a gangrenous appearance, and the general condition of the patient deteriorated. There was a high fever. During one of the dressings, when an attempt was made to pull away some of the gangrenous tissue, a large segment of

the alveolus came away with it. The resulting cavity had for its apex the cavity of the antrum of Highmore. There was a tedious convalescence, but healing eventually occurred by epithelization of the cavity. At the time of the patient's discharge from the hospital, there was a good deal of discomfort and disability while eating, because of this cavity, and the latter was therefore later occluded by a hard rubber obturator.

An empyema of the antrum of Highmore can also occur as a complication of a periapical abscess surrounding the roots of the appropriate

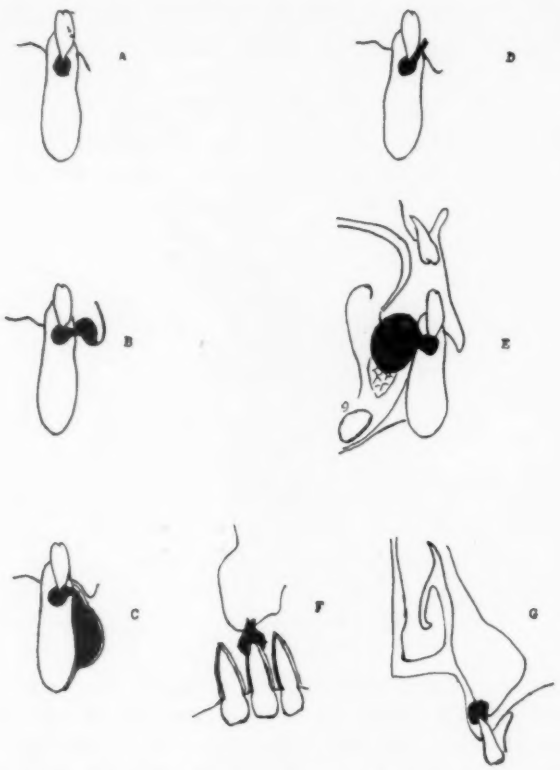

Fig. 4.—To show the lines of spread of a periapical abscess. *A* indicates a periapical abscess; *B*, a direct spread, gumboil type; *C*, a secondary "subperiosteal" type of pus pocket; *D*, follows pericementum and escapes at margin of gum; *E*, toward the tongue and in the floor of the mouth; *F*, points into the nasal cavity; *G*, perforates into the antrum.

teeth (fig. 4). Marshall and others also agreed that the anatomic basis of this lesion is a thrombo-embolic lesion of the apical arteries, the terminal branches of the superior dental artery as they enter to supply the substance of the teeth (fig. 1). In clinical practice, the differentiation is frequently impossible. Luckily, this is of no particular moment, because the line of treatment is the same.

Secondary involvement of the bone, originating in a sinusitis complicated by an empyema of the antrum of Highmore was observed by Lubet-Barbon and Furet. As a good deal of operating had been done, it is questionable whether the bone necrosis was not secondary to the operative manipulations rather than to the primary sinusitis.

4. A case of localization of the suppuration in the antrum, secondary to bone necrosis in the outer wall (canine fossa) of the maxilla, was reported by Halloran.

5. Cases are described in which the suppuration gathers behind the maxilla and extends upward as far as the base of the skull.

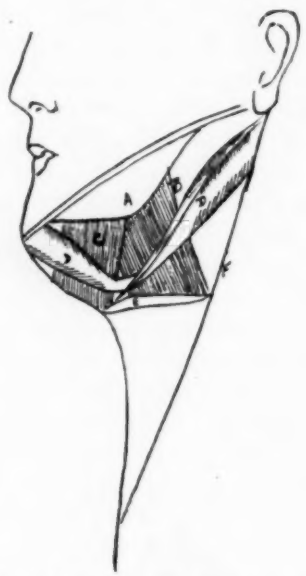

Fig. 5.—This shows the relationships of the lower jaw (*A*) to the mylohyoid muscle (*B*), the hyoglossus muscle (*C*), the digastric muscle (*D*), the hyoid bone (*E*) and the margin of the sternomastoid muscle (*F*). (After Gray.)

(*B*) Abscesses in relation to the lower jaw find the following general localizations:

6. On the outer side of the bone, they appear either in the interval between the cheek and the alveolus as gum-boils or larger abscesses, or, in relation to any part of the external surface of the bone—body or ramus—they burrow outward to localize in the subcutaneous tissue covering the lower jaw. Care is necessary in opening these abscesses not to injure the facial artery.

7. On the inner side of the lower jaw (fig. 5), the pus accumulates most commonly below the line of attachment of the mylohyoid muscle.

and the abscesses point in the submaxillary triangle. They should be opened externally. Less commonly the pus accumulates above the line of attachment of the mylohyoid muscle, and the abscess is then situated in the floor of the mouth to one side of the base of the tongue. These abscesses should be opened through the floor of the mouth.

8. Suppuration derived from an osteomyelitis of the angle of the jaw and in relation to the sockets of the last molar teeth usually burrows outward and points in the neck just below the angle of the jaw. If not opened soon enough, the abscesses spread forward around the posterior margin and in front of the mylohyoid muscle, and extend into the submaxillary triangle. Very occasionally, the abscess spreads further. If the spread occurs in front of the pretracheal fascia and anterior to the coalescence of the latter with the fascial investment of the great vessels (carotid sheath), the pus spreads downward in the anterior triangle of

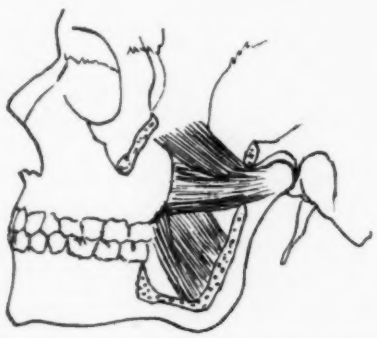

Fig. 6.—To show the origins and insertions of the external and internal pterygoid muscles and their relationship to the spread of any accumulations of pus. (After Gray.)

the neck, and may rupture or be incised and drained at any point above the clavicle. According to Marshall, cases are on record in which abscesses have discharged into the larynx and at points on the chest as low as the breasts.

9. Abscesses in relation to the ascending ramus of the lower jaw (fig. 6), on its inner aspect internally and anterior to the attachment of the pterygoid muscles point into the interior of the mouth far back and high up. Usually the inflammatory swelling is sufficient to ankylose the jaw more or less, and because of this fact the abscess is difficult to reach for the purposes of incision. The abscess usually breaks spontaneously into the oral cavity, and if one can find the opening, bare bone is invariably felt at the bottom of the sinus. Thereafter, the ankylosis, when due merely to inflammatory exudation, subsides slowly until full mobility is restored. Ankylosis, however, that is due to any calcification

in muscle or tendon, or to any new bone formation, is usually much more difficult to treat; full defervescence does not always occur, and complete ankylosis occasionally results.

On the inner aspect of the ascending ramus, pus that accumulates behind and to the outer side of the pterygoid muscles at their attachment to the lower jaw points in the interval behind the posterior margin of the jaw.

Pus that accumulates on the outer surface of the ascending ramus presents most of the physical characteristics of a parotid abscess. In incising the abscess, great care is necessary not to injure the branches of the facial nerve.

Large accumulations of pus are the rule with osteomyelitis of the lower jaw. These most frequently have the physical and anatomic characteristics of subperiosteal abscesses. As mentioned before (vide supra), sequestration does not always accompany these subperiosteal abscesses, although it quite commonly does. The anatomic relationships of the soft parts clothing the lower jaw of the muscles and their tendinous attachments, and of the planes of the various layers of the cervical fasciae, determine the path of spread of the accumulations of pus.

According to Gray, the cervical fascia consists of three layers: (1) a superficial layer, (2) a layer passing in front of the trachea, and forming with the superficial layer a sheath for the depressors of the hyoid bone and (3) a prevertebral layer passing in front of the bodies of the cervical vertebrae, and forming with the second layer a space in which are contained the trachea, esophagus, etc. The superficial layer forms a complete investment for the neck. It is attached behind to the ligamentum nuchae and the spine of the seventh cervical vertebra; above it is attached to the external occipital protuberance, to the superior curved line of the occiput, to the mastoid process, to the zygoma and to the lower jaw; below it is attached to the manubrium sterni, the clavicle, the acromion process and the spine of the scapula; in front it blends with the fascia of the opposite side. This layer would oppose the extension of abscesses toward the surface, and pus gathering beneath it would have a tendency to extend laterally. If the pus is in the posterior triangle, it might extend backward under the trapezius muscle; it might extend forward, under the sternocleidomastoid muscle; downward, it might extend under the clavicle for some distance, until stopped by the coalescence of the cervical fascia to the costocoracoid membrane. If the pus is contained in the anterior triangle, it might find its way into the thorax to become continuous with the pericardium; but, owing to the lesser density and thickness of the fascia in this situation, it more frequently finds its way through it and points above the sternum. The second layer of fascia

is connected above with the hyoid bone. It passes down beneath the depressors and in front of the thyroid body and trachea to become continuous with the fibrous layer of the pericardium. Laterally, it invests the great vessels of the neck and is connected with the superficial layer beneath the sternocleidomastoid muscle. Pus forming beneath this layer would in all probability find its way into the posterior mediastinum. The third layer (the prevertebral fascia) is connected above to the base of the skull.

BONE NECROSIS IN OSTEOMYELITIS OF THE JAWS

The physical characteristics of the area of bone necrosis that accompanies and follows osteomyelitis of the jaws, as in other bones of the body, vary directly with the size and importance of the vessel or vessels occluded by the osteomyelitic process.

(*A*) The blood supply of the superior maxilla is very abundant and is furnished by a number of moderately large vessels (the infra-orbital, the alveolar, the descending palatine, the sphenopalatine, the ethmoidal, the frontal, the nasal and the external maxillary vessels). Practically all of these vessels are derived from the trunk of the internal maxillary artery. The anastomosis is very free, and none of the arteries functions as an end-artery. The various aspects and areas of the maxilla that are supplied by the various vessels are fairly accurately indicated by their descriptive names. Practically the entire segment of the alveolar process is supplied by the alveolar branch of the internal maxillary artery and its continuation as the posterior dental artery.

A periosteal network is practically nonexistent; the little that corresponds to this is derived from an abundant network in the mucous membrane covering the alveolar process of the bone. The physiologic proof of this deficiency is found in the total absence of any new bone formation after disease or destruction of any part of the bone.

The interesting part of the blood vessel arrangement for the superior maxilla is found in the dominating fact that the entire supply is derived from one large arterial trunk, the internal maxillary artery, and that the branches enumerated previously, which form the network of supply, are arranged in loops based on the trunk of the internal maxillary artery. Study of figure 7 will amply demonstrate this fact. As an example, note the loop formed by the infra-orbital artery and the posterior dental artery by the interposition of the anterior dental branch of the former; or the loops formed by the gingival branch of the posterior dental artery with the nasal branch of the infra-orbital. It is as if a series of loops had their free ends gathered in a single bundle corresponding to the main trunk of the internal maxillary artery.

This simple anatomic fact explains adequately all the clinical forms of bone involvement and of bone necrosis that are found in osteomyelitis of the upper jaw, as follows:

1. Involvement of the entire bone with manifestations referable to the palatal, nasal and orbital surfaces results from a lesion in the stem of the internal maxillary artery prior to the giving off of the posterior alveolar branch with or without extension thrombosis in the loops described, which are derived from the internal maxillary artery. Collateral circulation is at a minimum, and a maximum lesion results.

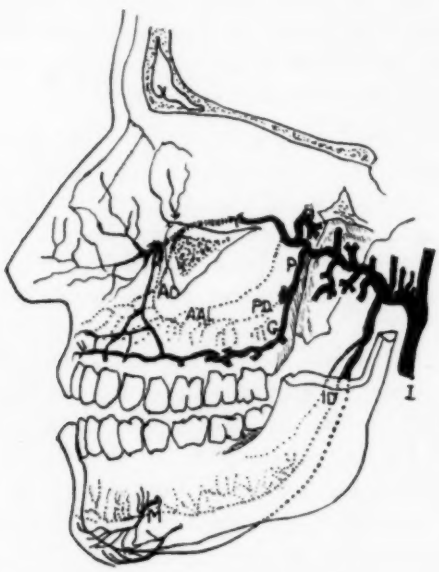

Fig. 7.—The blood supply of the superior maxilla. (After Deaver's Anatomy.) Study of this figure shows that the entire blood supply of the maxilla is derived from one large arterial trunk, the internal maxillary artery, and that the branches supplying the bone consist of, and are arranged as a number of, loops thrown around the bone at different levels and in different planes. For example, note the loop formed by the infra-orbital branch and the posterior dental branch by the interposition of the anterior dental branch of the former, etc. *I* indicates the internal maxillary artery; *P*, the posterior alveolar artery; *PD*, the posterior dental artery; *G*, the gingival branch of the posterior dental artery; *AD*, the anterior dental artery; *AAL*, the vascular loop from which the apical arteries are derived; *ID*, the inferior dental with its apical branches; *M*, the mental branch of the inferior dental artery.

2. Involvement of the alveolar process results from a lesion in the course of the posterior dental and gingival arteries. The amount of bone involved depends on the amount of collateral circulation.

3. Involvement of the anterior part of the alveolar process and the adjacent part of the bone results from a lesion in the course of the junction of the posterior and anterior dental arteries.

Involvement of the antrum of Highmore occurs with either group 2 or 3. The amount of bone involvement depends on the possibilities of collateral circulation.

4. Involvement of the palatal surface results from a lesion in the palatal arteries, or may be an extension from an involvement of the alveolar process.

5. Involvement of the nasal aspects of the bone results from a lesion in the nasal and anterior branches of the infra-orbital artery. This variety may also be associated with an empyema of the antrum of Highmore.

6. Involvement of the orbital aspect of the bone results from a lesion in the course of the infra-orbital artery.

Fig. 8.—To show some characteristic sequestrums that form from the superior maxilla. (See text.)

Sequestration in the superior maxilla corresponds to these areas of involvement and occurs in the following anatomic forms:

1. The usual sequestrums derived from the superior maxilla are small and of little or no importance, and ordinarily consist of small fragments from the margin of the teeth sockets, or larger segments extending more or less through the thickness of the socket and the alveolar process (fig. 8 *A, a* and *b*).

2. A characteristic sequestrum is found in the group described as occurring in nurslings and infants. The sequestrum involves practically the entire maxilla. The basis for this is anatomic (figs. 7 and 8 *C*).

Necrosis of the entire maxilla could be explained only on the presence of a lesion in the main stem of the internal maxillary artery prior to its division into the infra-orbital and posterior alveolar branches.

3. A sequestrum is seen which consists of the major portion of, or the entire, alveolar process, the separation or removal of which results

in laying bare the cavity of the antrum of Highmore. The anatomic basis for this must consist in a lesion (thrombo-embolic vascular occlusion) of the main trunk of the alveolar branch of the internal maxillary artery before its division into its component branches (fig. 8 *B*).

4. Rarely, the area of necrosis is limited to the nasal aspect of the maxilla (Menzel). The anatomic basis for this is a lesion in the branches of the anterior dental artery.

5. Rarely, the area of necrosis is limited to the outer side of the bone in the area contiguous to the zygoma (Halloran).

A case of this type occurred in a 60 year old man in whom an empyema of the antrum with high fever and an extensive cellulitis of the face developed, which compelled incision. Bare bone was felt in the canine fossa, and the finger broke through (fig. 8 *A, c*) easily into the antrum, demonstrating necrotic bone over a wide area extending backward and upward toward the root of the zygoma.

The anatomic basis for this type of sequestrum is a lesion in the appropriate branches of the infra-orbital branch of the internal maxillary artery.

Characteristic case reports are found elsewhere in this communication.

(*B*) The vascular arrangement for the inferior maxilla is as follows (fig. 7): The inferior dental artery penetrates the foramen on the inner side of the ramus of the jaw, and runs along the dental canal in the substance of the bone. Opposite the first bicuspid tooth it divides into two branches, incisor and mental; the former is continued forward beneath the incisor teeth as far as the symphysis, where it anastomoses with the artery of the opposite side; the mental branch escapes at the mental foramen, and anastomoses with the submental inferior labial and inferior coronary arteries. The dental and incisor arteries, during their course through the substance of the bone, give off a few twigs that are lost in the cancellous tissue, and a series of branches that corresponds in number to the roots of the teeth; these branches enter the minute apertures at the extremities of the fangs and supply the pulp of the teeth.

Collateral circulation is furnished from the opposite artery, and by its mental branch with the submental, inferior labial and inferior coronary arteries.

For my purpose this description may be paraphrased as follows: Each inferior dental artery acts as a nutrient artery for its appropriate half of the bone; it perforates the substance of the bone on the inner surface of the ascending ramus of its appropriate side, divides dichotomously and nourishes the bone up to the upper ends of the rami; in fact, the two inferior dental arteries are the nutrient arteries of the inferior maxilla. The upper ends of the rami are supplied from adjacent muscular branches.

The periosteal circulation is derived from numerous arterial trunks—muscular and otherwise—in the immediate neighborhood; it is most abundant over all parts of the bone except the upper part of the ascending ramus and its coronoid and condyloid processes. Here the periosteal structure disappears in the intimate rugged attachment of muscles, tendons and ligaments.

Sequestration of bone in the mandible as a result of osteomyelitis is characterized by being relatively small or grossly large (fig. 9).

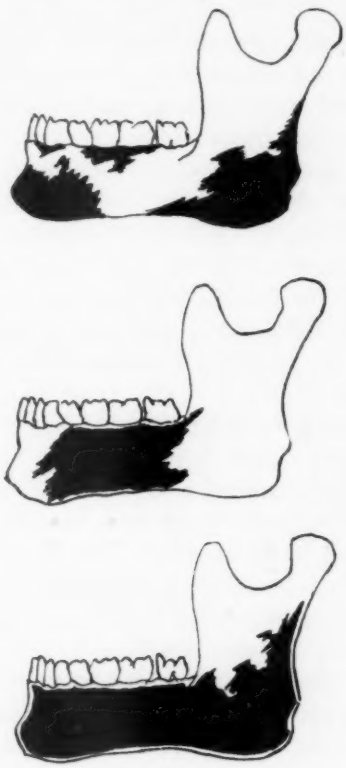

Fig. 9.—Types of sequestrums that form from the mandible.

Small and insignificant sequestrums limited to the margins of the teeth sockets are naturally common. Equally common, if not more so, are the large sequestrums that occupy relatively large extents of the mandible; these can be grouped as follows:

1. A variety in which the sequestrum occupies a large or major part of the body of the mandible.

2. A variety in which the sequestrum occupies the angle of the jaw and extends therefrom forward along the lower border of the mandible

and upward along the posterior margin of the ramus for a limited extent.

3. A variety in which the sequestrum is present at the point of the chin, usually displaying a tendency to extend more to one side than to the other.

4. A variety in which the entire body of the mandible forms the sequestrum; this includes the body, angle and lowermost parts of the ramus. Very rarely, this extends across the middle line and involves the opposite side.

The anatomic basis for these forms of sequestration is found in either the extension (odontogenous) or the metastatic (hematogenous) form of thrombo-embolic process in the inferior dental artery. The extent of bone deprived of blood supply by this process depends on the length of artery involved in the process, on the position of the diseased portion, with especial reference to its nearness or distance to the next nearest large anastomosing vessel (the inferior dental of the opposite side and the incisor and mental branches), and on the amount of collateral circulation. Because of the position of these anastomosing branches, blocking of the artery at any point proximal to these branches converts the artery into an end-artery, with all of its consequences up to the point of blockage.

The vascular arrangement for the upper half of the ascending rami of the mandible is as follows:

The coronoid and condyloid processes and the contiguous part of the ramus are supplied with blood by a number of arterial branches derived, for the most part, from the internal maxillary artery. This blood supply has very little collateral anastomosis with the blood supply of the remainder of the mandible, as represented by the blood supply derived from the inferior dental arteries.

Sequestration of the coronoid or condyloid processes of the ramus is uncommon. This probably has some relation to the great frequency of odontogenous factors in the production of osteomyelitis of the body of the lower jaw.

NEW BONE FORMATION IN OSTEOMYELITIS OF THE JAWS

As in other bones of the skeleton, the formation of new bone is an important element in the final healing and cicatrization of the bone wounds. New bone formation here, as in other bones of the body, is dependent to the largest extent on the presence of, and the anatomic structure of, the periosteum. As in both the upper and the lower jaw there is no true marrow cavity, any new bone formation derived from any endosteal osteoblastic cells is lacking.

(*A*) A small area on the anterior surface of the superior maxiila just below and in front of the malar process has a covering that approaches in structure that of a periosteal membrane. The membrane is continuous over the inferior orbital margin with the periosteum covering the floor of the orbit. The palatal surface and the alveolar process are covered with a thick mucoperiosteal membrane. The other surfaces of the bone are covered with the relatively dense attachment of muscles and tendons that find anchorage deep in the bone tissue, and in this respect the structure resembles that of the vertebrae. No periosteal membrane is present on these latter surfaces.

The important function of bone production under proper stimulus seems lacking in the upper jaw. Deficiencies of bone produced by disease, or otherwise, are not made good by bone tissue, but are repaired as best as nature may by ordinary fibrous tissue. Wherever the disease, by necrosis and sequestration, aided or not by operative removal of sequestrums, has resulted in the opening up of any accessory cavity such as the antrum, the defect remains; and either the latter is repaired by the coalescence of mucous membranes across the bared areas, or, as frequently happens, no covering takes place and the bared bone persists. At no time in clinical practice does one ever see the formation of involucrum at any point of the upper jaw. Repair in the sense of new bone production does not apparently exist.

(*B*) The lower jaw is clothed by a distinct periosteum at all parts except near and over the condylar and coronoid processes. Here the periosteal membrane becomes incorporated with the tendinous attachments of muscles and the fibrous structure of the ligaments of the temporomaxillary articulation. The periosteal circulation derives itself from numerous vessels in the immediate vicinity, is very abundant and furnishes the physical and physiologic basis for the involucrum, which forms under appropriate conditions about the lower jaw.

This faculty of bone production is well developed, and involucrum formation is abundant over all parts of the mandible except the upper parts of the ramus and its condylar and coronoid processes. In the latter locations, that is, in the neighborhood of the temporomaxillary articulation, a calcification occurs very commonly in the adjacent parts of the tendons and muscles attached to the coronoid and condylar processes; this should not be mistaken for the formation of new bone tissue.

COMPLICATIONS OF OSTEOMYELITIS OF THE JAWS

Lymphatic Drainage as a Complication of Osteomyelitis of the Jaws.—The cervical lymphatic glands frequently become swollen and tender, and commonly suppuration takes place in them. Schweitzer has

described the lymphatic drainage of both the lower and the upper jaw. This is best summarized in the attached table taken from his paper.

The Association of General Infection (Bacteremia, Sepsis, Septicemia) with Acute Osteomyelitis of the Jaws.—In osteomyelitis of the jaws, the clinical signs of a general infection may occur (*A*) at the onset of the illness or (*B*) later on, either as part of the essential pathology of the bone lesion or as part of some complicating condition.

(*A*) In the early cases it is most uncommon for the manifestation of the general infection to assume a dominant position, either immediately preceding or simultaneously with the onset of the local manifestations except in cases in which the hematogenous mechanism is well marked; such dominance occurs under the following conditions:

(*a*) In cases of specific infection, as in cases of typhoid, osteomyelitis of the jaw, etc., the general infection confines itself to the

Regional Drainage of Lymph Vessels of Upper and Lower Jaws

From the Region of	Upper Jaw Into Submaxillary Glands			Lower Jaw Into Submaxillary Glands		
	Ant.	Med.	Post.	Ant.	Med.	Post.
Incisors and canines	Only exceptionally one vessel	Almost ⅝	Almost ⅛	About ⅓	About ⅓	Occasionally
Premolars.....	0	Almost ⅔	Almost ⅓	Rarely	Almost all	0
Molars.....	0	Almost ½	A little more than ½	Occasionally 1 vessel	Almost all	Occasionally 1 vessel

characteristics it displays as a manifestation of the original illness, for instance, the typhoid fever. It is very uncommon for the general infection to assume the characteristics of a fulminating sepsis under such conditions.

(*b*) In cases following a previous local infection of the skin, as a furuncle, etc., the sepsis follows the forms customarily seen in clinical practice, and the clinical varieties vary from very mild to very severe forms of general infection.

The cases of acute osteomyelitis occurring in nurslings and infants that are rapidly fatal because of the intense toxemia belong in this group, as the infection is most probably introduced through some surface (skin or mucous membrane) injury, as indicated previously in the discussion. In one of Bass' cases, Staphylococcus aureus was recovered from the blood.

(*c*) In dental practice a general infection is almost invariably associated with some form of dento-alveolar abscess usually of the periapical variety. Acute and chronic forms of "septicemia" have been described (Marshall, Thibault and Raison and others). The chronic form corre-

sponds to one of the clinical entities, referred to usually under the general term of "focal infection" in this country, and is of no interest in relation to the subject under discussion.

The acute form of general infection is the one that is of interest in this article. According to Marshall, this form has been seen in dental practice in association with periapical abscess; and, as referred to previously, Marshall and others expressed the belief that all periapical abscesses are of hematogenous origin when there are no surface indications of the infection having been transmitted into the interior of the pulp chamber. When limited to the periapical space, these acute infections are commonly very mild, are without general manifestations and are forerunners of the chronic form of sepsis referred to in the previous paragraph.

In surgical practice the clinical course is different. Almost invariably the substance of the jaw bone proper becomes infected, and a severe form of osteomyelitis results which develops coincidently with the general infection. Forms are described in which a general infection occurs as a sudden, acute, overwhelming exacerbation of a previously existing focus of infection, usually a dormant periapical abscess, and without the intervention of any operative or other form of trauma. These forms are unusual. Much more commonly the general infection is associated with some operative manipulation indicated by some dental condition. The following two groups are met in clinical practice:

1. Following some operative manipulation—extraction of a tooth, treatment for a periapical abscess, etc.—it is uncommon to have postoperative fever of high magnitude with corresponding subjective and objective symptoms. Undoubtedly, excessive temperature of this kind must be referred to transient bacteremias with corresponding states of general infection of similar evanescence. Commonly the cases in this group go on to complete retrogression and recovery as regards the general and local condition.

2. There are, however, a number of cases of general infection that, originating as do the cases in the previous group, nevertheless, go on and show a steady progression, even to a fatality. The numbers of these latter cases are not correctly appreciated by the medical profession. I usually see one or two of such cases in hospital and private practice each year. General infections of this type, of dental origin and of operative mechanism, are apt to be of a high order of intensity and malignancy, to be complicated by intracranial complications, and to be rapidly fatal within a very few days.

B. General infection occurring as a late phenomenon in the course of osteomyelitis of the jaw follows some form of trauma, either that occurring during a dressing of the wound, or that following operative

intervention. Clinically, general infection at any late stage of the disease, under the conditions specified, follows the form of development indicated in the immediately preceding two paragraphs (1 and 2) and with similar consequences.

Under any of these conditions, complicating nearby or distant lesions occur as a result of the transmission of the infecting bacteria through the blood stream. Some of these possible secondary conditions are also capable of being associated with a general infection. Commonly, one is faced with a combination of conditions, in which the general infection can be referable to either the original jaw infection, or its complication, as, for instance, a cavernous sinus thrombosis or a meningitis. Positive and negative blood cultures may be obtained in otherwise equally severe and fatal cases.[2]

In hematogenous cases and in those in which secondary general infections take place, metastatic foci can and do develop as a result of the bacteremia. Indeed, in some of the hematogenous cases the jaw lesion itself may be only one of many manifestations. These include (*a*) other bone lesions, (*b*) suppurative and nonsuppurative forms of arthritis, (*c*) infections of the various body cavities, (*d*) forms of endocarditis and pericarditis, (*e*) lung abscesses, (*f*) renal infarcts and (*g*) minor abscesses in the various fascial planes. These are common to all forms of hematogenous infections, and further discussion of them is beyond the scope of this paper.

Local Complications.—A group of complications occurs, which take place because of local extension of the disease. These complications include:

(*a*) The various abscess formations, including orbital abscess and empyema of the antrum, have been discussed previously. Rather uncommon complications that result from the pointing and rupture of the cervical forms of abscess include those described in the literature in which rupture took place into the larynx or trachea, or those that extended into the thorax.

(*b*) Ankylosis of the temporomaxillary articulation occurs as a result of involvement of the glenoid process in the lesion, or as a result of calcification of the muscular and tendinous tissues about the joint and upper part of the ascending ramus. This includes various forms of arthritis of the temporomaxillary articulation.

(*c*) Lesions about the angle and body of the lower jaw can rarely cause a phlebitis of the facial vein radicals, which, when once estab-

2. The significance of positive and negative blood cultures in clinical practice in cases of acute infection has been discussed on another occasion (Wilensky, A. O.: Treatment of Infection: General Principles Underlying Treatment from a Surgical Standpoint and Therapeutic Indications to be Drawn Therefrom, Arch. Surg. **15**:737 [Nov.] 1927).

lished, has a predilection for spreading upward into the cavernous sinus. I have the records of one private case, have seen one case in hospital practice and have seen one report in the literature. The last is reported by Coppens:

A man, aged 21, a wood-worker, except for a fracture of the arm and an attack of typhoid fever many years before, had never been ill. Fifteen days before admission he became suddenly ill with excruciating pain in the left lower jaw, with high fever, delirium and other signs of a general infection. Incisions were made in the gingivo-labial fold which gave little relief and showed a process in the lower jaw, but the illness was progressive thereafter until the patient died.

Postmortem examination showed an entire denudation of the entire left side of the lower jaw. The bone was necrotic and gangrenous; the process seemed to stop anteriorly at the median line, and to extend up to the temporomaxillary articulation. All the veins that have their point of origin in the inferior maxilla were full of pus; the external jugular vein was also full of pus, and the pus was traced up into the left cavernous sinus. The right side was healthy. A meningitis was also present.

(*d*) A very rare complication is meningitis. Coppens' patient also had meningitis.

(*e*) Sinus disease (empyema of the antrum of Highmore, usually with, and sometimes without, involvement of the major portion of the frontal, ethmoidal and sphenoid sinuses) complicates osteomyelitis of the upper jaw. Encephalitis appears as a secondary complication. Halloran's case was an example of this:

As indicated in another part of this communication, Halloran's patient had osteomyelitis of the upper jaw with an empyema of the maxillary sinus and roentgen evidence of pansinusitis. After drainage, the patient left the hospital in a much improved condition, only to return five weeks later with a progressive development of bilateral labyrinthine symptoms. At the peak of development, there were bilateral paralysis of the eighth nerve and paralysis of the left seventh and twelfth nerves. Laboratory tests gave essentially negative results. Improvement occurred in the manifestations referable to the seventh nerve; the paralyses of the eighth were still persistent at the time of Halloran's report.

(*f*) Marchand mentioned cases of cerebral abscess that were reported as complications of osteomyelitis of the jaws. Under these conditions, cerebral abscess represents a further development of an encephalitis.

(*g*) In common with other wounds, wounds resulting from osteomyelitis of the jaws may be complicated by erysipelas and by tetanus.

TREATMENT

The general principles governing the treatment for acute osteomyelitis in general have been described on several previous occasions and will not be repeated here. For the present purpose suffice it to say

that cases of osteomyelitis of the jaws can be divided into the following groups:

Cases with clinical signs of a general infection.
Cases with few or no signs of a general infection, but with various grades of the local lesion.
Cases with complications.

As in previous parts of this communication, the odontogenous factors relating to the subject will be incorporated in the discussion as the occasion arises.

Cases with Clinical Signs of a General Infection.—1. Highly fulminant forms of general infection are usually of such a high order of severity as to render useless any form of local or general treatment. The group includes: (*a*) highly toxic cases occurring in nurslings and infants, (*b*) hematogenous cases following local surface (skin, mucous membrane, etc.) forms of infection in which the jaw lesion may be only one of several metastatic foci and (*c*) certain of the military injuries. Cultivations of the peripheral blood are practically always positive in the cases in this group. The prognosis is uniformly bad, and fatalities are to be expected.

2. In very sick patients with high fever and other clinical signs of general infection, cultivations of the peripheral blood are usually negative. Retrogression of the infection is common in the cases in this group spontaneously and occasionally as a recognizable partial or complete result of the form of treatment employed. However, a fatal outcome may occur subsequently either because of an intensification of the infection and a change from a sterile condition of the blood to one of bacteremia, or because of the occurrence of local or distant complications. The cases in this group include: (*a*) some of the severer cases of osteomyelitis following trauma and fracture of the jaw; (*b*) some military injuries and (*c*) cases of acute infection of the jaw following operative manipulation. In the latter cases, treatment should be persistently directed to the local condition, as detailed subsequently in this communication.

Cases with Few or no Signs of a General Infection, But with Various Grades of the Local Lesion.—The cases in this group consist of the bulk of the patients seen in practice, in which the problem is that of the local lesion and its local complications, principally abscess formation, and in which the question of general infection does not enter. In these cases the treatment resolves itself down to the best ways and means that will lead to the minimum loss of tissue, to the most rapid shedding of the sequestrums, to the most rapid healing of the wounds, to the greatest conservation of form and function and to the best general advantage to the patient.

Common accumulated experience and the literature make it evident that for the local lesion the general practice of conservation is the accepted principle of treatment at the present time. This is in accord with the theoretical considerations of the subject that I have made on several different occasions, and with which I am in complete accord. In lesions of the upper jaw, conservatism has been forced on the surgeon because of local anatomic and technical considerations; in lesions of the lower jaw, this has come about because of experience.

Ordinarily, the treatment for the local lesion itself should be considered under the following headings: (1) prophylaxis, including the treatment for any antecedent condition, (2) treatment for the local condition in the early stages and (3) treatment in the later stages.

(1) Effective treatment for any antecedent condition is necessary when the osteomyelitis follows some form of trauma and when it is associated with an odontogenous condition. It is beyond the scope of this communication to consider the traumatic conditions of the jaw (fractures, gunshot wounds, operative procedures, etc.) that are complicated by osteomyelitis.

The odontogenous conditions are, however, important, and adequate attention to them includes certain prophylactic measures.

Prophylaxis is the most important single item in the prevention of any local infection of the jaw bones from odontogenous sources. Generally speaking, the best one can do in regard to any form of general infection is also purely of a preventive nature. Most of the cases seen in practice are in association with odontogenous factors and occur as a result of unwise dental procedures or as unexpected consequences of apparently necessary manipulations even in very capable hands. The most important means at hand lie in the field of dental prophylaxis, which would tend to avoid, to decrease in numbers or to wipe out completely any form of dental infection. The importance of this simple means cannot be overemphasized, and fortunately this means of prevention of disease is being recognized more and more thoroughout the country. The next most important means of prevention of local or general infection lies in closer attention to the rules of asepsis in dental practice among the rank and file of the dental profession, and to appreciation of the great importance of gentleness in all dental procedures. For practical purposes, this comprises all that one can do especially in cases of general infection, because when once the infection has occurred, cure and healing depend on the relationship of individual resistance and the virulence and intensity of the infecting organisms; over this interaction of natural forces medical knowledge has little control at present.

Cases are well known, especially to the dental profession, in which apparently spontaneous exacerbations of infection extending into the

tissues of the jaw bones occur in previously existing periapical forms of dento-alveolar abscess. Efficient prophylaxis would prevent these accidents also, except in those cases in which the periapical abscess is itself manifestly a manifestation of a hematogenous infection.

In actual practice, infection of the jaws occurs as a complication of the following dental procedures:

(*a*) The extraction of teeth. It is a common practice among the dental profession to pack the teeth sockets after extractions. This one item accounts, in my opinion, for a very large proportion, if not the vast majority, of infections of the jaw, as the corking up of the secretions in the cavity of the tooth socket practically forces the infection into the bone tissue of the jaw. The dental profession should avoid this step, and should accept the policy of nonpacking after extractions as a prophylactic measure.

(*b*) The treatment for dento-alveolar abscesses of purely odontogenous extent and limitation. This, also, is a prolific cause for infection of the jaw bones. Many times infection of the jaw occurs because of the mere presence and the nature of the infecting organism and the lack of general and, especially, local resistance of the patient and the tissues. But here, again, infection is equally often aided materially by the lack of aseptic technic and by the lack of gentleness in the manipulations. For periapical abscesses, extraction of the tooth is the simplest and most common treatment; naturally, the prophylactic considerations detailed in the previous paragraph are applicable with increased force when infection is present.

The majority of periapically infected teeth do not require anything further than clean extraction. Curettement through the socket of the extracted tooth appears to me not only questionable but totally unadvisable. The apical contents, by such a procedure, are usually thoroughly macerated with the normal blood clot and remain in the socket, thereby creating an excellent culture tube. The bone curet in the hands of an unskilled operator is a dangerous instrument, especially so when that operator feels called on to curet all sockets after extraction, whether the case is an acute alveolar abscess or not. Many cases of osteomyelitis are the result of this form of treatment.

(2) Once an acute osteomyelitis has established itself in the bony tissues, it is important to recognize that in the early stages a period of extraordinary virulence of infection is present, usually lasting a very few days, during which any active or radical measures are likely to be productive of much harm, especially in the spread of the local infection and, possibly, even, as pointed out previously, in the production of a general infection. The importance of absolute conservatism throughout this stage is paramount.

In the presence of odontogenous conditions, no extraction should be made at this stage, nor should any other dental procedure be carried out. In the presence of any other preceding trauma or operation, due regard should be had to the dangers of causing an increased exacerbation of the infection and the possible creation of a general infection by the trauma incident to any dressing of the wound; certainly, under such conditions no further operative procedure should be undertaken, and any absolutely necessary dressings of the wound should be carried out most gently and with knowledge of the danger well in mind. During this stage of increased virulence, only the simplest measures necessary to proper cleanliness of the mouth should be practiced, and the contraindication to extraction or further manipulation should be absolute.

Benevolent change from the period of increased virulence is manifested by a lessening of the swelling of the tissues of and about the jaws, and by a perceptible decrease in the general and other local manifestations of bacterial infection. Any necessary dental condition that needs correction should be taken care of at this time, and in actual practice the procedure should be strictly limited to the extraction of definitely diseased teeth from which the local lesion apparently originated. The value and importance of the extraction lie in the fact that removal of the diseased tooth allows free drainage from any associated form of dento-alveolar abscess, and, by not doing anything else and, especially, by leaving the socket free from packing, it can be confidently expected that the odontogenous lesion will quickly and progressively retrogress thereafter. In cases of other etiology—especially operative cases—the policy of conservative passivity should be persevered in during this stage also.

In hematogenous infection of the jaws, the policy of conservatism during the early stages of development of the jaw lesion seems to me to be also of extreme importance. In these cases, the general principles underlying the treatment for acute osteomyelitis in general hold good, and, as so often happens in osteomyelitis of the irregular bones, this attitude is fortified and made imperative by anatomic and local technical considerations.

Sooner or later, in any of the varieties of acute osteomyelitis of the jaws, suppuration occurs; in most of the cases, the paths and localizations of these accumulations have been detailed in a previous part of this communication. From the point of view of efficient incision and drainage of these abscesses, the following classification is possible (see section on "Suppuration with Osteomyelitis of the Jaw," p. 206):

(*a*) In abscesses tending to point in the mouth, every effort should be made to drain as many of the abscesses as possible through the mouth. Many of the smaller abscesses, especially those of the gum-boil type, and those occurring in nurslings and infants spontaneously point and

rupture in the oral cavity, and no further attention is necessary besides efficient cleanliness. Other types of abscesses need incisions, which follow the usual surgical practice; abscesses of the cheeks can be reached in the angle between the cheek and the gum. Included in this group are all of the ordinary abscesses that form in association with the upper jaw on its palatal, alveolar and external aspects. As Marx pointed out, even some of the orbital abscesses and those forming on the face near the inner canthus of the eye can be reached from in front of the jaw by tunneling beneath the cheek from the reflection of the buccal membrane.* In the lower jaw, the group includes all of the abscesses that gather above the line of attachment of the mylohyoid muscle and in front, and to the mesial side, of the pterygoid muscles; appropriately placed incisions in the floor of the mouth or at the buccal reflections will adequately care for these accumulations of pus.

(*b*) Abscesses that gather behind the upper jaw, or in relation to the condylar processes of the lower jaw, accumulate in inaccessible situations where incision is difficult. Practically, it is safer and better for one to await their spontaneous pointing and rupture into the mouth behind the palatal processes, or in front of the anterior margin of the ascending ramus of the mandible high up, than to attempt any incision; the danger of these inaccessible abscesses spreading in the reverse direction, especially upward toward the base of the skull, is, while known, negligible in practice.

(*c*) Abscesses in relation to the lower jaw and arising from lesions below the line of attachment of the mylohoid or pterygoid muscles proceed, as was pointed out previously in this communication, in the general direction of the submaxillary and anterior triangles of the neck when the lesion is anterior to the angle of the jaw. The general rules applicable to the proper incision and drainage of abscesses of the neck in these locations apply here and need no repetition. It is important not to open these abscesses too soon, and it is equally important not to open them too late, in order to prevent tracking of the pus for any considerable distance downward toward the thorax, or inward toward the larynx and trachea, as was described under exceptional circumstances by Marshall and others.

(*d*) Abscesses in relation to foci at the angle of the lower jaw characteristically accumulate below and behind the angle of the jaw and tend to point there. The best incision for this accumulation is an angular incision below and behind the angle of the jaw; frequently, perfect drainage is possible by a stab wound and a large rubber tube drain just below the angle, when the abscess is sufficiently soft and large.

(*e*) Orbital abscesses should be treated most conservatively, as it is the rule for them to rupture spontaneously and for no disturbance

of vision to result. When the accumulation of pus spreads upward into the superior parts of the orbital cavity, incision is necessary and should be made through or under the eyelid. Healing occurs uneventfully.

(*f*) Antral accumulations of pus invariably discharge through the natural duct. It is practically never necessary in nurslings and infants to open the antrum from without, as abundant drainage results through the duct and through the sockets of the molars as these are exfoliated. In rare cases in adults, removal of any offending teeth is necessary, and the antrum must be effectively drained. Usually this can be done through the socket of the appropriate teeth; occasionally a much wider opening is necessary, and the latter should be made in the outer wall of the antrum above the alveolar border.

In acute osteomyelitis in infants, the extensive pathology includes most of the items and conditions included in this communication. In spite of its extent, conservative measures are best: hot fomentations in the beginning; cleanliness of the mouth and the nares; careful watching for presenting abscesses and their immediate opening, so that as little as possible in the way of disfiguring scar or deformity results; the avoidance of external incisions by clever and efficient care of orbital and antral complications; the withdrawal and removal of sequestrums and, above all, careful nursing and abundant nourishment; all of these are important in the final outcome of those who do not succumb to the initial general infection.

Commonly any of these abscesses is associated with much induration in the tissues in and about the jaw, and the emptying of the abscess nevertheless leaves a good sized swelling, which slowly disappears spontaneously and more quickly when aided by poulticing. The important rule to remember, however, is that no attempt should be made at the time the abscess is opened to execute any procedure on the bone itself; usually any such attempt is followed by increased swelling and induration, if by nothing more dangerous.

(3) The late stages of acute osteomyelitis of the jaws are characterized as the period in which sequestration occurs. The causes for this and the physical and anatomic characteristics of the various forms of necrosis have been detailed in previous parts of this communication. Efficient separation of the necrotic portions of the bone usually occupies from thirty to ninety days, depending on the area of necrosis and other local conditions. During this period suppuration is apt to be profuse both through the external sinuses and through the sinuses in the oral cavity about the teeth. Retention of pus is common, and new closed-off pockets may, and do, commonly, form, which need additional incisions. It is important to remember that during these incisions the aim should be to restore or create proper drainage for the accumulations of pus,

and on no account should any interference be made with the bony structure. The reasons for these precautions include:

(*a*) One is unable to recognize and distinguish adequately between necrotic and healthy viable bone, except through the plane of separation between healthy and dead bone.

(*b*) Sequestration, especially in the cases of more moderate extent, does not occur, or occurs in such small or limited extent as to be negligible; when of such small or limited extent, nature will take care of and properly exfoliate such sequestrums very much better and with less damage than can be done by the surgeon. In many of these cases, the pathology is that of a subperiosteal abscess pure and simple.

(*c*) When appreciable areas of bone necrosis occur, they are of minimal size commensurate with the position of the thrombophlebitic lesion and of its consequent disturbance of blood supply, when the natural process of sequestration is allowed to go on undisturbed.

(*d*) If interference with the bone structure is practiced at too early a stage, it most commonly results in an increase of the lesion and of the area of necrosis.

(*e*) In the lower jaw, the importance of waiting is paramount for the purpose of allowing sufficient involucrum to form so that the form and configuration of the lower jaw and the chin are retained. In the upper jaw, this consideration does not exist, as involucrum does not form.

These, too, are the considerations and reasons that decide the advisability of delaying the sequestrotomy until conditions are most favorable, so that no untoward consequences follow and so that the greatest conservation of form and function may be preserved.

Under such restrictions and conditions, the process of sequestration and its unaided or operatively aided exfoliation is reduced to its simplest form. Many times the sequestrum will be spontaneously discharged, or, during one of the dressings, a sequestrum presenting in the mouth of one of the sinuses can be easily withdrawn almost without the patient's knowledge; healing then proceeds quickly and efficiently. Both of these methods of termination are common for acute osteomyelitis of the jaw.

When some operative procedure is necessary for the removal of the sequestrum, the following simple rules should be remembered:

1. Whenever possible, and to as large an extent as possible, the operation should be done through the oral cavity.

2. Enlargement of any preexisting wound should be practiced only commensurate with the size of the sequestrum.

3. Chiseling away of any involucrum for this purpose should be done to the minimum degree, and should be so planned that the minimal

amount of deformity results. As a rule, very little of this is necessary. As was indicated previously, this applies practically exclusively to the lower jaw.

4. Any manipulation through the oral cavity or from the outside should be carried out in such fashion that a minimum amount of trauma is done to the muscular and tendinous tissues about the condylar and glenoid processes of the mandible, in order to prevent any calcification of these tissues and a consequent ankylosis of the temporomaxillary articulation.

5. Any external incision should be planned with due regard to a minimum of resulting visible scar.

6. Any necessary drainage should be instituted as far as possible from the inside of the mouth, and in the largest number of cases this can be done exclusively so. Then one can neglect any open sinuses that present externally, and it usually follows that the external openings promptly close.

Healing after secondary operations is usually a protracted affair, and the average case extends over a period of three or four months before complete closure is secured. Occasionally revisions are necessary, and during these procedures much the same rules should be followed. The important rule to remember is that the less one is forced to do, the less damage one is apt to do, the better for the local condition, and the quicker will be the subsequent healing.

Fry called attention to the frequency with which pathologic fractures occur in osteomyelitis of the mandible. This has not been so in my own experience. The diagnosis is made on the basis of deviation of the mandible from the midline to the affected side, crepitus and roentgen findings. The amount of displacement depends on the line of fracture, the presence of teeth on the smaller fragment with occluding teeth on the maxilla, and the amount of loss of bone. The general principles underlying the treatment are correct alinement, reduction of sepsis and immobilization of the fragments.

Dental splints should be fitted as early as possible to immobilize the fragments and thereby relieve the pain, reduce the danger of sepsis and allow the patient to take food more easily. Early surgical intervention by wiring or plating is contraindicated. Reduction of sepsis may be accomplished by constant irrigation, efficient drainage and the removal of septic teeth and teeth in the line of fracture. Splinting is used to aid the reduction of the displacement and to immobilize the parts. Immobilization is obtained by means of bandages and external supports, interdental wiring (of which there are four varieties) or dental splints.

In cases of osteomyelitis of the upper jaw even extensive necrosis does not necessarily mean extensive deformity, and one is constantly

surprised at the little change that is perceptible in the contour of the cheek and face. When the antrum has been exposed, healing is accompanied by epithelization of the cavity; the opening usually contracts but little, and commonly remains permanently. It is necessary to have an obturating appliance made to close the opening, and use can be made of the obturator to carry artificial teeth to replace those missing. Symptoms referable to the orbit disappear with the subsidence of the process and the healing of the lesion. Nasal symptoms usually need local attention for a little time, especially when, as so often happens, they are associated with disturbance in the antrum.

In cases of osteomyelitis of the lower jaw the involucrum results in an appreciable thickening of the jaw; the amount of deformity is, however, small. Dental appliances are necessary to make good the teeth that have been destroyed by the disease or as a consequence of operative manipulation.

When large portions of the jaw are lost, the remaining fragments are drawn toward each other by the contraction of the muscles, and the teeth are thrown out of occlusion, producing in many cases a great deformity, especially when the chin is swung to one side. To prevent this, it is necessary to keep the remaining portions of the jaw immobile and in proper alinement by fixation of the teeth in their normal occlusion. The simplest method is interdental ligation. Sometimes, because of a lack of teeth, a splint may be necessary, or even a vulcanite bar may be placed in the wound to maintain contour until new bone has formed; this bar can be removed and cleaned, and also can gradually be reduced in size as new bone is formed.

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A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.
LOS ANGELES

E. STARR JUDD, M.D.
ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.
ROANOKE, VA.

JEAN VERBRUGGE, M.D.
ANTWERP, BELGIUM

ADOLPH A. KUTZMANN, M.D.
LOS ANGELES

ALEXANDER B. HEPLER, M.D.
SEATTLE
AND
ROBERT GUTIERREZ, M.D.
NEW YORK

KIDNEY

Anomalies.—Tachot [1] reported 12 cases of congenital malformation of the kidney. At nephrectomy the right kidney, which had been excreting purulent urine, was mistaken for the vena cava. The kidney resembled a long, cylindric sausage and ran from the bony pelvis to the normal renal region, at the right side of the aorta, just where the vena cava should be. An exploratory puncture elicited a brownish-red liquid, partly colloidal silver and partly blood, indicating that the organ was a kidney. Above the bladder the caliber of the sausage-shaped structure suddenly diminished and became a ureter slightly larger than normal and 5 cm. long. There was no true pedicle, and the vascular connections were so numerous and the denudation of this long tube so difficult that its extirpation required three hours. Embryologically it is explained that when the definitive kidney was formed, the nephrogenous mass presented adhesions with the twenty-third, twenty-fourth and twenty-fifth somites, preventing it from mounting in its entirety as the ureter progressed upward. The latter, crowned with a particularly plastic mass of renal tissue and meeting no obstacle to its ascent but the adhesions, arose to its normal place, carrying with it as much of the kidney as was free to rise, pulling it upward in this remarkable formation.

1. Tachot: Pathology of the Kidney Affected with Congenital Malformation, Arch. d. mal. d. org. gén.-urin. **6**:253, 1931.

The frequency of renal malformation suggests that, before proceeding to any operation on the "reno-ureteral" system, it should be determined whether there are two kidneys and whether they are in normal position. Neither the presence of two ureteral orifices at the two angles of the trigone nor the division of the urine with different concentrations of urea and different color is an infallible indication of the presence of two kidneys. In the diagnosis of renal disease the possibility of malformation must be considered, and significance attached to the presence of concomitant anomalies of the genitalia, which should always be thoroughly examined. The only true proof of the presence of the condition is obtained by roentgenographic and pyelographic examinations.

Donohue [2] stated that the relief of obstruction of the upper part of the urinary tract with conservation of both kidneys is rarely accomplished in cases of horseshoe kidney. In the majority of reported cases, one kidney is generally found injured to such an extent as to require resection. In a recent case reported by Donohue, hydronephrotic changes were moderately advanced in one kidney as the result of obstruction at the ureteropelvic juncture. The obstruction was relieved by division of the isthmus connecting the two kidneys. Postoperative examination in this case has shown that the affected kidney has returned to normal.

Hess [3] reported a case of adenocarcinoma in a horseshoe kidney; the patient was a man aged 56. Resection on the right side was done. The vessels of the renal pedicle were abnormal in number, and were ligated and cut individually. A large piece of muscle was transplanted over the surface of the stump at the lower pole of the remaining kidney. The patient recovered from the operation. On examination a growth about 8 cm. in diameter was found. The diagnosis was adenocarcinoma.

[COMPILERS' NOTE.—A comparatively large number of tumors in anomalous kidneys, particularly of the horseshoe type, has recently been reported. Several cases of squamous cell tumor associated with stone have been found at operation. Apparently deficient drainage of the renal pelvis and an abnormal location, subjecting it to trauma, make the kidney more susceptible to infection, formation of stone and tumor.]

Jacobs [4] reported a case of ectopic pelvic kidney which was treated by nephrectomy. An unmarried woman, aged 25, complained of dysmenorrhea and abdominal tumor. Exploratory laparotomy revealed an ectopic kidney. Because the presence and condition of a second kidney had not been determined, the abdomen was closed and cystoscopy was

2. Donohue, P. F.: Division of Horseshoe Kidney for Relief of Ureteropelvic Junction Obstruction, J. Urol. **27**:59 (Jan.) 1932.

3. Hess, Elmer: Adeno-Carcinoma Horseshoe Kidney, J. Urol. **27**:47 (Jan.) 1932.

4. Jacobs, Arthur: Renal Ectopy, Brit. J. Urol. **3**:432 (Dec.) 1931.

done, which revealed a normal right kidney and a left pelvic kidney. Although no other abnormality was present, the kidney was removed to obviate hazard in a possible future pregnancy and to relieve the dysmenorrhea.

The incidence of renal ectopy is about 1 in 660 persons. It must not be confused with nephroptosis, which, although the predisposing factors may be congenital, is acquired. Renal ectopy is an embryonic developmental defect associated with vascular anomalies which check the upward migration of the kidney from the bony pelvis where it is situated in its earliest stages of development. It also fails to rotate, so that urography reveals the characteristic short ureter and the pelvis directed anteriorly instead of laterally. These observations, together with the anomalous vessels found at operation, which fix the kidney in an unusual position, distinguish the condition from nephroptosis. Its recognition is important because it simulates other abdominal conditions, and if the patients are women the abnormally situated organ may seriously complicate pregnancy and parturition.

[COMPILERS' NOTE.—Jacobs' case obviously is one of simple ectopia, that is, an embryogenic anomaly associated with the kidney lying at a lower level than normal, a blood supply arising from the aorta at a lower level than normal and a short ureter. At times the vascular pedicle may even arise from the iliac arteries and not infrequently from the aorta below its bifurcation. Because of the fixation of the kidney and its inadaptability to suspension, the preoperative diagnosis of ectopia in contradistinction to nephroptosis should be emphasized. A consideration of possible ectopic kidney is necessary in distinguishing tumors in the lower part of the abdomen from those in the pelvis. Interference with gestation is a frequent concomitant of iliac or pelvic ectopia. Under such conditions nephrectomy may be indicated. Ectopic kidneys are frequently poorly developed, often malformed and the seat of infectious or calculous disease.]

Tumors.—Alessandri [5] stressed the importance of the various means of roentgen diagnosis of tumors of the kidney. Simple roentgenography often shows the renal contour if the colon has been well emptied. Pyelography and urography with iopax are also useful. The injection of oxygen into the perirenal fat and pneumoperitoneum has been practiced by the author for several years. Four cases, 1 of renal carcinoma, 2 of hypernephroma and 1 of tubular carcinoma of the kidney, in which the latter methods made diagnosis possible, are reported in detail.

Because of the danger of producing emboli through rough handling of hypernephromas at operation, Alessandri devised a special incision

5. Alessandri, R.: Accorigimenti clinici e operativi per la diagnosi e la cura dei tumori del rene, Ann. ital. di chir. **10**:41, 1931; abstr., Am. J. Cancer **15**:3023 (Oct.) 1931.

which affords room to ligate and section the renal vein before freeing the tumor, even if it is large. The incision consists of a longitudinal limb, beginning at the costal margin just within the anterior axillary line and extending downward, and a transverse limb extending from the upper end of the longitudinal limb backward along the twelfth rib, which is resected.

[COMPILERS' NOTE.—So far as we know, injection of oxygen into the perirenal fat as an adjunct to roentgen diagnosis in urology is an innovation. Preliminary ligation of the renal vein as a one or two stage procedure in nephrectomy for tumor is, of course, a common practice in America. This is usually carried out through a transperitoneal incision or a Bazy modification of the Mayo lumbar incision. The incision described by Alessandri is novel in American practice.]

Jacobs and Hoffman [6] stated that a tumor invading the retroperitoneal perirenal fossa, when of the mixed cell sarcoma type, is highly malignant; myxomas, although only locally recurrent, are equally malignant. Treatment consists of complete extirpation of the kidney and tumor, including the adipose capsule. The perirenal fat should also be dissected from the peritoneum and from the muscles of the posterior abdominal wall. Radium and deep roentgen treatment at the site of nephrectomy should be applied immediately. The expectancy of life in these cases is less than one year. Recurrences at the original site are common and are immediately followed by generalized metastasis.

Crosbie and Pinkerton [7] reported the case of a woman, aged 35, with malignant leiomyoma of the kidney. The right kidney, which contained the tumor, was removed under spinal anesthesia, and convalescence was uneventful. The tumor occupied, roughly, the position of the pelvis and had greatly thinned the kidney over a large area at the upper pole. Microscopically, the tumor was found to be a leiomyoma originating in the outer wall of the pelvis. The authors stated that if this tumor had remained in the body, it might have become clinically malignant within a relatively short time. Propitious removal indicates that the prognosis will probably be favorable.

Dean and Pack [8] studied the cases of 16 patients with embryonal adenosarcomas of the kidney treated at the Memorial Hospital. Excluding the 1 adult in the series, the average age was 3 years. These tumors originate at different periods in the development of the embryo. One of the first symptoms of the disease is usually the accidental

6. Jacobs, L. C., and Hoffman, L. H.: Rare Renal Tumors, J. Urol. **27**:33 (Jan.) 1932.

7. Crosbie, A. H., and Pinkerton, H.: Malignant Leiomyoma of the Kidney, J. Urol. **27**:27 (Jan.) 1932.

8. Dean, A. L., Jr., and Pack, G. T.: Embryonal Adenosarcoma of the Kidney, J. A. M. A. **98**:10 (Jan. 2) 1932.

finding of a tumor in the abdomen, although pain, asthenia, malaise, hematuria or polyuria may be the initial evidence of the condition. When a large mass is palpable, the disease is widespread and the prognosis is unfavorable. The lesion generally extends by direct infiltration, but metastasis may occur through venous or lymphatic channels.

Surgical treatment of these tumors is unsatisfactory because of the tendency to recurrence. Although the growths are highly radiosensitive, irradiation alone has not effected cure; it does cause marked regression of the tumor and amelioration of symptoms in most cases, however. The authors are of the opinion that primary Wilms tumors should be treated by external irradiation. As soon as the growth has largely or wholly disappeared, nephrectomy should be performed. Metastasis or local recurrences are best treated by external irradiation.

Lieberthal [9] reported 7 cases of malignant tumors of the kidney of children. He stated that large abdominal tumors in infancy are usually malignant tumors of the kidney, the majority being mixed tumors of the embryonal adenosarcoma group. In lesions of this type sections should be taken from each part of the neoplasm in a search for the typical epithelial groups which will identify the tumor as an embryonal adenosarcoma. Inability to demonstrate these epithelial groups does not exclude the possibility that the tumor belongs in this group.

Embryonal adenosarcomas arise from the metanephros. The neoplastic change of the latter may occur at any stage in its development from the the mesodermal stage, where it is present only as metanephric anlage, to the point where actual metanephros has already differentiated. The earlier origin may be ascribed to cases in which striated muscle is present and the later origin to cases in which it is absent. The glomerulus-like structures in these tumors represent true embryonic glomeruli. The most significant symptom of malignant renal tumor of children is a rapidly growing, painless abdominal tumor. Hematuria is usually absent.

The general consensus among most surgeons is that treatment should be surgical, regardless of the size of the tumor, provided metastasis or severe cachexia is not present. Otherwise, death will occur within a year after the tumor is discovered. The youth of the patient is not a contraindication to operation. Israel reported a successful operation on an infant aged 3½ months, in which a tumor filling two thirds of the abdomen was removed. In a series of 20 patients not operated on observed by Albarran and Imbert, 14 died within six months, 3 within one year and 3 after one and a half years; only 1 survived three years. Death from recurrences and metastasis after operation

9. Lieberthal, Frederick: Malignant Tumors of the Kidney in Childhood: A Report of Seven Cases of Embryonal Adenosarcoma, Surg., Gynec. & Obst. **53**: 77 (July) 1931.

usually occurs within the first year, and it may occur as late as the fifth year. Israel advised a five year period of observation before considering a patient cured. Albarran and Imbert found the operative mortality to be about 25 per cent, although the total early and late mortality, including deaths due to recurrences and metastasis, reaches 86 per cent.

The median line incision was used in the cases reported by Lieberthal and is favored by most operators, as it enables better exploration of the abdomen for metastasis and aids in determining whether the tumor is bilateral. Israel favors the retroperitoneal approach, the line of incision following the long axis of the tumor. Voelcker's incision begins in the costovertebral angle and extends to the umbilicus; the peritoneum is opened widely.

[COMPILERS' NOTE.—Malignant tumors of the kidneys of children are rapidly fatal, and therefore the prognosis is poor. Most of the tumors appear during the first two years of life. They cause few symptoms. The pelvis of the kidney is generally not involved; consequently, hematuria and urinary obstruction are uncommon, and pain is rare. In the early stages the growths are small, firm, freely movable, localized to the region of the kidney and painless. When the tumor is moderately large, it often retains the contour of a normal kidney. The duration of symptoms is usually short before death occurs. Walker, in a series of cases in which operation had not been performed, found the average period of life after the onset of symptoms to be eight months; following nephrectomy the average period of life was sixteen months. In an occasional case the period of symptoms and growth of the tumors extends for several years.

The structure of the tumor is characteristic histologically. Many varieties of tissue have been described, but the predominating structures are groups of incompletely formed glands, surrounded by masses of irregularly disposed cells of an appearance somewhat similar to that of the cells forming the glands. They may contain striated muscle, squamous cell nests and more rarely areas of bone and cartilage. Magoun and McCarty stated that the growth is composed of one type of cell in various stages of differentiation and with varying amounts of connective tissue reaction. They classified the tumors as carcinoma of the adenomatous type. If metastasis or local extension has occurred, operation is often rapidly fatal. Death is certain if operative intervention is not carried out. Nephrectomy in most cases prolongs life and offers the patient the only chance of improvement. Earlier writers agree on the very high mortality.]

Rumpel [10] stated that the first objective changes in renal tumors consist of alterations in the contour of the kidney and its function.

10. Rumpel: Zur Diagnose die Nierentumoren, Zentralbl. f. Chir. **58**:751, 1931; abstr., Am. J. Cancer **15**:3023 (Oct.) 1931.

Subjective symptoms may be lacking or late in appearance. The function of the kidney, as measured by sodium indigotin disulphonate, U. S. P. (indigocarmine), is decreased following hematuria in cases of renal tumors. The function returns slowly to normal after the bleeding ceases. This phenomenon occurred in all the cases examined by Rumpel. Retrograde pyelography is preferred to the intravenous type in cases of tumor, and repeated examinations should be carried out in early cases to avoid error in diagnosis.

Stones.—Szenkier [11] stated that the diagnosis of nephrolithiasis is usually not difficult since a fairly definite syndrome is present. Infection of the appendix and gallbladder increases the difficulties of differential diagnosis when the calculus is on the right side. Blood cells in the urine, while suggestive of renal stone, have also been observed in cases of appendicitis. The Goldflam sign, or the elicitation of pain in the loin by a forceful blow, is not always pathognomonic, as it can also be elicited in other conditions such as a retrocecal appendix, pyelonephritis and renal tuberculosis. Occasionally the roentgenograms do not reveal the presence of renal stones.

Head's zones of hyperesthesia following renal attacks were mentioned. It has been observed only in cases of nephrolithiasis that, on grasping the abnormal side, the pain appears transmitted to the opposite side, similar to Guyon's renorenal reflex. Former explanations of the latter phenomenon compared it to sympathetic ophthalmia or the toxins of the diseased kidney affecting the normal side. By the work of Vernets and Mones it has been shown that there is an inferior mesenteric plexus in human beings. This solitary plexus is common to fibers from both kidneys. It is found in front of the aorta, at the juncture of the inferior mesenteric artery and aorta. To this plexus come the sympathetic nerve fibers of both kidneys, which call forth the following possibilities in cases of nephrolithiasis: (1) Pain stimuli originating in the diseased kidney go to the central plexus and give rise to pain in that kidney; (2) pain stimuli from the diseased kidney go through the plexus and into the segmental vertebral sympathetic fibers and then, stimulating the outer spinal segments, cause areas of hyperesthesia of the skin on the diseased side (Head's areas); (3) pain stimuli from the diseased kidney go through the plexus and call forth pain sensations in the normal kidney on the opposite side (renorenal reflex), and (4) there may be elicited both renal pain and areas of hyperesthesia on the sound side. It is Szenkier's belief that, although this sign of elicited pain referred to the sound side is not infallible, it can be of much aid in diagnosing nephrolithiasis.

11. Szenkier, D.: Ein neues Symptom der Nephrolithiasis, Ztschr. f. Urol. **25**: 250, 1931.

Weber [12] stated that three factors are significant in explaining the formation of urinary calculi: the mode of living, infection and urinary stasis. There may also be other unknown factors involved, particularly in cases of lithiasis occurring coincidentally with disease of the bone. Stone not uncommonly occurs in cases of disease of the bone complicated by infection, such as comminuted fractures, chronic vertebral ankylosis and infectious arthritis.

The following cases were mentioned: bilateral calculus associated with an amputation of both thighs; passage of sixteen stones following ankylosis of the hip of long duration, together with much infection; left renal calculus developing after fracture of the femur complicated by infection and the formation of a sequestrum. There were several cases of coxitis, as well as a case of involvement of the bladder following injury, in which urinary calculus resulted. In a case of simple tibial fracture the bone did not unite in six months, and later calculi of the urinary tract developed.

Weber is of the belief that sudden inactivity as the result of a fracture lowers the usual carbon dioxide exchange and affords an opportunity for it to combine with the calcium salts, resulting in the formation of stone.

[COMPILERS' NOTE.—Weber's observations on the incidence of urinary lithiasis and disease of the bones are noteworthy. From time to time reference to such association has been made, but it has been difficult to establish any causal relationship. One would presume that infection might play an important part in spite of Weber's contention that a metabolic disturbance of the carbon dioxide exchange is at fault.]

Eisenstaedt [13] considered certain etiologic factors in the formation of urinary calculus. Urinary stasis, from whatever cause or wherever situated, is significant; infection of the urinary tract is subsequent to and dependent on this condition. If the infecting organism is a urea splitter, the likelihood of formation of stone is markedly increased.

In a series of fifty-five stones examined, the nuclei contained bacteria, which appear to be material factors in their production. The hydrogen ion concentration of the urine is significant and seems to be a factor in the precipitation of urinary salts. In cases of lithiasis the hydrogen ion concentration of the urine obtained from the diseased side is usually higher than that from the healthy side. Recent experimental work indicates that the so-called protective urinary colloids may not be as important as supposed. Deficiency of vitamin A seems to be an indirect

12. Weber, W.: Steinbildung und Knochenerkrankungen, Ztschr. f. Urol. **25:** 36, 1931.

13. Eisenstaedt, J. S.: Certain Tangible Factors in the Etiology of Urinary Calculus, Surg., Gynec. & Obst. **53:**730 (Dec.) 1931.

contributing factor in the experimental formation of calculi, producing increased susceptibility to infection in general and particularly in the urinary tract.

[COMPILERS' NOTE.—Eisenstaedt's comment that urinary stasis is a significant factor in formation of stone is generally accepted by other observers. Stagnation invites the stone-forming process and enhances the chance for deposition of stone-building material. The significance of bacteria in the nuclei of stones is not so clear, nor can we agree that the part played by hydrogen ion concentration has been properly established as a causal factor. Furthermore, what we do know of the mechanism of formation of calculus is definitely linked with the colloidal solvent mechanism of the urine or its imbalance. The mechanism whereby deficiency of vitamin A produces stone is yet to be determined. Not yet can it be stated definitely that this type of formation is or is not associated with infection. This could well be the next point of attack on the problem.]

Hydronephrosis.—Walters [14] stated that most cases of hydronephrosis are the result of definite obstruction at the ureteropelvic juncture. The causes of such obstructions are usually anomalous renal blood vessels, peripelvic connective tissue causing angulation or collapse of the ureter, narrowing of the ureter at the ureteropelvic juncture due to subepithelial fibrosis and obstruction of the ureteropelvic juncture due to lateral insertion of the ureter. The indications for conservative surgical procedures for hydronephrosis are limited to cases in which the hydronephrosis involves both kidneys, or in which it involves one kidney of which sufficient parenchyma remains to justify preservation of the organ.

Fourteen cases in which removal of the obstruction had been combined in some instances with nephrostomy and nephropexy were considered. Whether division of anomalous blood vessels obstructing the ureteropelvic juncture can be performed without too much disturbance of the blood supply to the kidney should be determined before they are severed by temporarily occluding them by means of a rubber-covered hemostat. After division of the anomalous vessels, the ureteropelvic juncture must be at the dependent portion of the pelvis, and the pelvis must be drained efficiently or symptoms of obstruction will continue. Resection of the renal pelvis has been performed in cases in which the pelvis was greatly dilated, and the laterally inserted ureteral orifice was collapsed with the distention of the renal pelvis. In these cases resection was carried out so that when the pelvis was closed, the ureteral orifice became dependent, adequately draining the kidney.

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14. Walters, Waltman: Evaluation of Results of Conservative Surgical Treatment of Hydronephrosis, Proc. Staff Meet., Mayo Clin. **6**:712 (Dec. 2) 1931.

Postoperative complications that may occur are obstruction at the ureteropelvic juncture, with retention of urine in the renal pelvis; infection of the renal parenchyma, with formation of cortical abscess, and extravasation of urine about the kidney. The various operative procedures carried out by Walters have given satisfactory results as measured by the following effects: disappearance of symptoms of obstruction of the urinary tract, such as pain and fever; return of the size of the renal pelvis and calices to within normal limits; absence of retention of urine in the kidney, and improvement in renal function subsequent to operation.

[COMPILERS' NOTE.—The conservative surgical attack on the pelves of hydronephrotic kidneys is one of the developments of recent years. The contributions of Quinby, Walters and others to this work are stimulating and promising. Recently Young described a procedure whereby the renal pelvis is resected in this manner and its remainder so sutured that it is drawn away from the constricting anomalous vessel without the latter being sacrificed. The emphasis placed by Walters on the establishment and maintenance of drainage of the renal pelvis at its most dependent position at the conclusion of the operation is noteworthy. This seems to be the important point in the procedure.]

Tuberculosis.—Caulk [15] stated that renal tuberculosis is less common because of early diagnosis and improved treatment of pulmonary and general tuberculosis and the prevention of massive lesions. Early diagnosis in renal tuberculosis is paramount.

In unilateral renal tuberculosis, nephrectomy should be performed promptly. The immediate relief of symptoms in many of these cases after operation is due to the removal of a tuberculin reaction created by the products of bacteria, tuberculoproteins, fats and fatty acids. Often the more acute the lesion in the bladder, the more quickly the healing and relief of symptoms follow removal of the diseased kidney. The possibility of healing in chronic renal surgical tuberculosis is remote and not comparable to that of simple early experimental lesions. The mortality of nephrectomy for this condition is low, and relief of vesical symptoms may be expected in at least 75 per cent of cases of unilateral renal disease, whereas invalidism is almost inevitable if patients are left to medical care. A comparison of the results in patients with renal tuberculosis treated by nephrectomy and in those treated expectantly indicates the ineffectiveness of medical treatment. Parsons, in 1925, pointed out that 85 per cent of the patients treated medically were dead within five years. Wildbolz, in 316 cases in which no operation was performed, found that 58 per cent of patients died within five years and only 6 per cent lived more than ten years. Of 104 patients on whom he performed nephrectomy for renal tuberculosis, 55.7 per cent were

15. Caulk, J. R.: Renal Tuberculosis, J. Urol. **26**:189 (Aug.) 1931.

completely well at the end of ten years. Sutter reported 61 per cent well between eleven and seventeen years after operation. In 863 cases at the Mayo Clinic, 58.1 per cent of patients were cured four years after operation. In Caulk's series of cases, 56 patients (51.9 per cent) have been traced. Forty-three (77 per cent) of these are well and free from vesical symptoms; 23 per cent still manifest evidence of the disease or have died.

In cases of bilateral renal tuberculosis, surgical procedures are indicated only in cases of emergency to relieve the patients of toxemia from pyonephrosis or to correct intractable vesical lesions.

[COMPILERS' NOTE.—Operation for early unilateral tuberculosis of the kidney receives a challenge from time to time. The contributions of Thomas on this subject in the last few years are noteworthy. Caulk, however, voiced the opinion held probably by most urologists, that under such conditions nephrectomy is the procedure that offers the greatest possibility of cure. Operation for certain reasons may be contraindicated, but those who advocate medical treatment should bear in mind that temporizing with unilateral renal tuberculosis may lead to such extension of the tuberculous process that the patient will ultimately be subjected to greater operative hazard in an attempt at cure.]

Hunt [16] stated that primary renal tuberculosis probably never occurs, as the kidney alone is seldom the site of tuberculosis. It is a rather common surgical lesion of the kidney, constituting 28 per cent of the lesions for which nephrectomy has been done in Hunt's experience.

Ten years ago it was generally accepted that nephrectomy was the preferred treatment in cases of unilateral renal tuberculosis. Even with evidence of associated tuberculosis elsewhere in the body in approximately 80 per cent of cases of renal tuberculosis, the patient should not be deprived of the benefit to be obtained by removal of the major tuberculous lesion, provided the latter is unilateral renal tuberculosis. Nephrectomy was justified in such cases because of the low primary mortality rate of about 2 per cent, even though there was moderate pulmonary involvement. Bilaterality of the disease was a distinct contraindication to nephrectomy, unless acute unilateral complications were present. In the presence of associated tuberculosis, nephrectomy was only a part of the treatment.

Medlar recently concluded that the kidneys of patients dying of pulmonary tuberculosis are commonly involved. In his experimental work with animals in which miliary tuberculosis was produced, it has been shown that renal tuberculosis is common in the guinea-pig and that bilateral involvement is the rule. Thomas, in 57 per cent of the cases in

16. Hunt, V. C.: When Should a Tuberculous Kidney Be Removed? West. J. Surg. **40**:40 (Jan.) 1932.

which renal tuberculosis existed, found bilaterality of the disease, and stated that since all renal infection in which bacilli of tuberculosis are present is hematogenous in origin, both kidneys are infected equally, and that bilateral infection is the rule.

Two years ago Hunt reviewed 838 cases of renal tuberculosis observed at the Mayo Clinic during the period from 1919 to 1929 to determine approximately the incidence of bilaterality of the disease. Nephrectomy was performed in 574 (68 per cent) of these cases. In the 264 cases in which operation was not done, nephrectomy was advised for but refused by 43 patients. The operability by nephrectomy was 73 per cent. In the remaining 221 cases, a definite diagnosis of bilateral involvement was made in 91. From the clinical evidence a diagnosis of bilateral renal involvement was made in only 111 (about 13 per cent) of the entire series. Wildbolz reported a mortality rate of 40 per cent within ten years, stating that more than half of the deaths were due either to tuberculosis of the remaining kidney or to tuberculosis elsewhere. Braasch had previously reported 20 per cent of deaths within five years after operation from similar causes. Assuming that half of these deaths may have been the result of tuberculosis of the remaining kidney, Hunt is of the opinion that a primary or late incidence of 25 per cent bilateral involvement is a liberal estimate in renal tuberculosis.

Perinephritic Abscess.—Fowler and Dorman [17] stated that perinephritic abscesses are usually classified as primary and secondary. In the primary group are included all cases in which the primary focus of infection lies outside the kidney. In the secondary group the primary lesion is in the kidney, the perirenal tissues becoming infected secondarily as a complication or sequel of the renal disease, either by direct extension from or rupture of the primary focus. This occurs particularly in cases of pyonephrosis, either calculous or tuberculous. From the standpoint of diagnosis the secondary group is not so significant. The primary renal lesion is the one requiring attention, and usually is readily recognized by urologic study; the treatment is directed primarily to the intrarenal lesion.

Fowler and Dorman considered the so-called primary or metastatic type of the disease. It is evident from a study of the reported cases that staphylococci are the infecting organisms in an overwhelming majority of cases of true perinephritic abscess. Multiple abscesses may form secondarily in various tissues and organs, such as bones, lungs, kidneys and muscles. In children the bones are most frequently infected by acute osteomyelitis; in adults infection of the kidneys is the most significant complication. It has been shown experimentally that trauma is instrumental in the development of perinephritic abscess. A history of injury is frequently obtained in these cases.

17. Fowler, H. A., and Dorman, H. N.: Perinephritic Abscess, J. Urol. **26**: 705 (Dec.) 1931.

There is no pathognomonic sign by which an early diagnosis can be made. Pain is generally a constant early symptom, coming on quite suddenly and without reference to the patient's activity. It may be severe or of a mild, dull aching type. It is definitely localized over the affected kidney and usually not referred. The majority of abscesses are situated posteriorly to the kidney, producing the maximal point of pain or tenderness in the costovertebral angle. Fever of the septic type is present in all cases, the temperature varying daily as much as 4 degrees. Signs of sepsis soon accompany these symptoms. The urinary findings are usually negative.

Diagnosis should be made as soon as possible in order that destruction of the kidney as well as other complications, sepsis and abscess of the lung may be avoided. Recent infections such as boils, carbuncles, paronychia, tonsillitis and infections of the skin should be carefully noted.

Free drainage should be established in every case as soon as a positive diagnosis is made. The usual oblique lumbar incision should be employed, with ample space to explore the kidney easily and thoroughly. After the main abscess is opened and drained, a careful exploration of the parts should be made with the finger to make sure that all pockets are freely opened and drained. Exploration of the entire kidney to rule out multiple abscesses will often hasten recovery and prevent subsequent operation. Cases of tuberculosis, pyonephrosis or multiple cortical abscesses may require nephrectomy. This is best performed later, after thorough drainage has been established with subsequent cleaning of the wound.

[COMPILERS' NOTE.—The danger of overlooking perinephritic abscess in cases of obscure sepsis is called to attention frequently. The insidious onset, the variable degree of pain and the absence of urinary symptoms often serve to deceive even an astute clinical observer. Emphasis is placed on care to determine the presence of pain in the costovertebral angle. The use of the exploratory aspirating needle is advocated by some, and if carried out with due care not to injure the pleura or viscera seems to have a place in diagnostic procedure. With the establishment of a probable diagnosis, surgical exploration and drainage as advocated by Fowler and Dorman is the operation of choice. Nephrectomy, if necessary, may be better carried out at a later date when the condition has become chronic. The main points in the diagnosis of perinephritic abscess are tenderness in the costovertebral angle, obliteration of the border of the psoas muscle, leukocytosis, intermittent fever and, at times, a history of previous infection of the urinary or extra-urinary tract. In late cases there may also be a slight curvature of the spine away from the infected side.]

URETER

Anomalies.—Lepoutre, Laurent and Berthelot [18] stated that it was impossible to discover an extravesical outlet of the ureter in the male before urethrocystoscopy came into use, and the only reported cases were found at necropsy. In the male an outlet into the posterior urethra does not cause incontinence of urine, since the abnormal ureter never opens in front of the verumontanum. It is revealed only by an infectious complication, the abundance and intermittency of the pyuria serving as guides. If urine is replete with pus over a period of months or years, it can be explained only by pyelorenal suppuration. Examination of secretion expressed from the prostate gland determines how much infection comes from this gland. If the urine is perfectly clear from time to time, the pyuria must have its origin above. In the majority of cases anomaly of the ureter is accompanied by a double kidney and duplication of the ureter on the affected side. The presence of an abnormal orifice in the posterior urethra is brought into view by the urethrocystoscope, and a catheter passed into this will elicit a liquid similar to urine. This ureter, the terminal extremity of which passes through an inextensible organ, subject to congestive attacks, is greatly exposed to dilatation and infection, and the associated kidney has a precarious future. Frequently the abnormal portion of the urinary system is transformed into a vast ureteropyonephrosis. If the kidney is single, the treatment is like that for any other form of pyonephrosis. If the kidney is double, an effort should be made to remove only the diseased portion. If the lower part of the ureter is not removed and is infected, it will become the source of new disturbances. The lower part of the ureter should be resected to the point where it enters the prostate gland. Otherwise, it will require subsequent operation.

[COMPILERS' NOTE.—The problem of an ectopic ureter opening extravesically has been thoroughly considered in the literature from the embryologic and clinicopathologic points of view. Dossot of Necker Clinic tabulated from the literature 154 unusual cases, 46 of which occurred in males. Clinically, it has been demonstrated that since there is no sphincter action at the mouth of the ectopic ureteral orifice there is always ascending infection, causing dilatation of the whole upper part of the urinary tract. The association of other anomalies is also common, and the proper treatment, whenever this condition is determined by urographic methods, is the combined method of ureteronephrectomy, or, if a double kidney is present, ureteroheminephrectomy.]

18. Lepoutre, C.; Laurent, G., and Berthelot, J.: Outlet of the Ureter into the Prostatic Urethra, Arch. d. mal. d. org. gén.-urin. **6**:310, 1931.

Gibson [19] reported a case of supernumerary ectopic ureter. The patient was a man, aged 20, who had persistent pyuria. Urography showed a left double kidney, the uppermost pelvis of which was dilated and communicated with the posterior urethra by means of an enormously dilated, tortuous ureter. The lower pelvis opened normally into the bladder. There was also an unusual anomaly of the fifth lumbar vertebra and the sacrum. The whole left side of the sacrum was oversized and the left innominate bone was considerably larger than the right. There was a tilt in the lower part of the dorsal spine apparently due to anomalous wedging of the dorsal vertebra.

Gibson concluded that the case emphasized the significance of congenital anomalies as an immediate or predisposing cause of pathologic conditions arising in the genito-urinary tract, and illustrated the frequent association of anomalies of the urinary tract with other anomalies. A thorough urologic investigation should be carried out in all cases of pyuria which do not respond to medical treatment. Treatment is usually heminephrectomy, including ureterectomy.

A series of 100 cases of ureteral ectopia was reviewed by Kilbane in 1926, and in 1928 Thom, of Bier's Clinic, reviewed 185 cases. In 1930 Sargent reported a case of ureteral ectopia and found that of 186 patients, 123 were females and 63 males, a ratio of approximately 2:1. It was noted that the condition of most female patients was diagnosed during life, whereas practically all male patients came to necropsy. This is due to the fact that ureteral ectopia of the females is accompanied by incontinence, since the ureters open either within the external urethra or vulva or within the vagina or uterus, causing constant urinary leakage in spite of normal urinary function.

Tumors.—Chauvin and Cerati [20] reviewed from the literature 112 cases of primary ureteral tumors, to which they added 4 of their own. Men were more often affected than women; the ages varied from 22 to 90 years, with the highest incidence at 60. The incidence of calculi varies from 21 per cent (Albarran) to an incidence of 5 in 35 cases reported by Kretschmer. Leukoplakia in the upper part of the urinary tract is relatively rare as compared with its occurrence in the oral cavity. It was associated with only 8 cases in this series. The distribution of the tumors anatomically is reported as being even with respect to the two sides. The most common site of the new growth is at the normal points of ureteral constriction, namely, the two extremities and the brim of the pelvis. The tumors in this series were usually single and

19. Gibson, T. E.: Supernumerary Ectopic Ureter, West. J. Surg. **39**:280 (April) 1931.

20. Chauvin, E., and Cerati: Les tumeurs épithéliales primitives de l'urétère, Arch. d. mal. d. org. gén.-urin. **5**:631, 1931; abstr., Am. J. Cancer **15**:3028 (Oct.) 1931.

small. Metastasis was noted in only 5 cases, and in each instance different organs were involved. It is believed that the mechanical difficulties due to the presence of the tumor cause death in most cases before metastasis can develop. Local extension and implantation in the lower part of the ureter and trigone of the bladder occur more frequently. The benign papillary growth was noted in 36.6 per cent of the cases. Of the malignant neoplasms, papillary carcinoma was the most common; 20 were atypical, infiltrating growths and 8 were basal cell carcinomas.

Hematuria was the main symptom. The prognosis is grave, even in benign papilloma, on account of a serious renal complication.

Stones.—Dourmashkin [21] stated that there are many cases in which stones are passed that never come to the attention of a physician. Cystoscopic manipulation was carried out in practically all of his series of 565 cases.

Cystoscopy is indicated in all cases of acute renal retention in order to establish drainage and thereby prevent infection. It was possible to pass the obstruction in 114 of 137 cases of acute renal retention in Dourmashkin's series. The urine escapes through the catheter with great force, sometimes in a continuous stream. Although only a small percentage of cases shows evidence of severe renal infection as a result of obstruction by stone, the best method to combat the infection is through the establishment of drainage by means of an ordinary catheter. Unless the stone protrudes from the ureteral orifice the passage of catheters in acute cases is sufficient. Metallic dilators, rubber bag catheters or other massive instruments should not be used during an acute attack. The indwelling catheter is of great value in acute cases. Including the chronic cases, it was used in 237 cases in this series. Its usefulness is limited in chronic cases in which the calculus is usually large, because ordinary catheters do not produce sufficient dilatation to allow the stone to pass. In acute cases the catheters may be left indwelling from one hour to several days. In chronic cases the proper application of the modern technic of cystoscopy may result in the reduction of open operations, especially when the stone is situated in the lower end of the ureter. In these cases the calculus usually measures more than 0.5 cm. in width and there is a history of repeated attacks of renal colic. The stone in these cases is arrested on its way down because of impaction and relative narrowing of the ureter, and treatment should be directed toward the removal of these obstacles.

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21. Dourmashkin, R. L.: The Basis for Management of Ureteral Calculi: Based on the Study of Five Hundred and Sixty-Five Cases, J. A. M. A. **98**:276 (Jan. 23) 1932.

Ureteral meatotomy was performed in 104 cases. It may be considered a harmless procedure, although in 1 case an alarming hemorrhage ensued from its use.

At least a week should be allowed to elapse between treatments. If the dilation has been ample and little if any edema is present, the stone may pass from the ureter without colic; ordinarily the expulsion of the stone is preceded by an attack of renal pain.

In 1,467 cystoscopic manipulations, including the initial examination, there were no deaths. In 100 cases in the entire series, stones more than 0.6 cm. in diameter were passed without operation. The advantages of cystoscopic manipulations are mainly economical.

[COMPILERS' NOTE.—Dourmashkin reported a fairly large series of cases with no mortality, and, as he expressed it, the main advantages of this type of removal of ureteral stones are economical. On the other hand, not infrequently several attempts are necessary to remove the stone, in some cases associated with much discomfort. It must not be forgotten that the risk is also small following the open operation for removal of ureteral stone. In a report of 640 cases of ureteral stone removed by operation, published in 1925, there were only 4 (0.62 per cent) deaths. There were no deaths following uncomplicated ureterolithotomy. In the 4 cases in which death occurred, either other surgical procedures were also carried out, or other disease of the urinary tract was partly responsible for the death.]

Obstruction.—Young [22] stated that obstruction at or near the ureteropelvic juncture is not infrequently caused by vessels which pass from the great vessels to the lower pole of the kidney. Two cases are reported in which these vessels caused an acute flexure, kinking and obstruction of the ureter, bilateral in one case and unilateral in the other. In the bilateral case the less affected kidney was operated on first. The aberrant vessels obstructing the ureter were clamped, divided and ligated, after which there was a postoperative reduction in the function of the kidney on this side. Drainage of a huge hydronephrotic sac was continued for more than a month by means of a retained ureteral catheter passing out through the penile meatus. This resulted in restoration of the kidney to practically normal function, so that it was possible to save it and to carry out the conservative plastic operation on the pelvis with excellent results. At the second operation Young performed a new procedure by means of which it was possible to resect the redundant pelvic sac and, in closing it, to draw the ureter

22. Young, H. H.: Obstructions to the Ureter Produced by Aberrant Blood Vessels, Surg., Gynec. & Obst. **54**:26 (Jan.) 1932.

away from the veins so as completely to remove the possibility of obstruction. A satisfactory result was obtained in this case. The same procedure was done in the second case, with complete success.

Transplantation.—Coffey [23] reported on the origin and progress of his method of transplantation of the ureters into the large intestine. The principle on which his operation is based is that of the physiologic valve which permits the delivery of fluid from a duct in which the pressure is low into a hollow viscus in which the pressure is high. The valve, which must be distinguished from a sphincter, is produced by the duct running for some distance in the wall of the hollow viscus before it enters the lumen. The importance of this arrangement in preventing regurgitation of contents and dilatation of the duct was discovered during experiments on pancreatectomy in which transplantation of the common bile duct into the intestine was necessary.

Coffey's operation has been modified and improved so that three distinct procedures have been developed. The first procedure consists in drawing the ureter into the interlamellar space immediately beneath the intestinal mucosa, its split end being drawn through an opening made in the mucosa at the caudal end of an uncompleted intestinal incision and anchored inside the intestine; thus the open ureter is brought into the intestinal lumen at the time of operation. One ureter is transplanted at a time to allow for the subsidence of edema. It is the method most frequently used because of its priority and applicability to exstrophy of the bladder in children. In the second procedure a tube or catheter is fastened within the ureter by ligatures which both seal the ureter against intestinal infection and anchor it to the catheter; after this the catheter is passed through an opening made in the mucosa at the caudad end of an uncompleted intestinal incision, and is used to draw the ureter into the interlamellar space beneath the intestinal mucosa and through the opening in the mucosa into the intestinal lumen. The urine is transmitted from the upper part of the ureter through the catheter into a receptacle outside the body. The anastomosis is completed, and the open ureter exposed to intra-intestinal pressure only after the intra-intestinal end of the ureter sloughs and permits the catheter to come away, from eight to sixteen days after operation. The development of this technic has greatly increased the indication for ureterorectostomy because it is applicable when the ureters are dilated and when there is a single kidney, but mainly because it permits the simultaneous transplantation of both ureters at a single operation. It is the method of choice in carcinoma of the bladder, vesico-

23. Coffey, R. C.: Transplantation of the Ureters into the Large Intestine. Submucous Implantation Method, Personal Studies and Experiences, Brit. J. Urol. 3:353 (Dec.) 1931.

vaginal fistula and intractable bilateral renal tuberculosis. In carcinoma of the bladder in the male, total cystectomy may be combined with this operation with little additional risk. In the female this is not practical, and destructive doses of radium may be applied or the bladder may be removed at a second operation.

The third procedure is still in the experimental stage. Because of its simplicity it will probably supplant the first procedure in cases of exstrophy of the bladder. Only one ureter can be transplanted at a time. The ureter is brought into the interlamellar space outside the intestinal mucosa by an anchor stitch which fastens the end of the ureter in the angle of the caudal end of an uncompleted intestinal incision. The anastomosis is gradually made by a tightly tied suture which transfixes both the ureter and intestinal mucosa. The anastomosis is complete three or four days after operation.

It is apparent that with these operations there should be a high ultimate mortality because it is inherent in the conditions for which the operation is performed. In cases of carcinoma it will depend on the type of cases accepted for treatment. In the hands of a skilled abdominal surgeon the operative mortality should not exceed 5 per cent. Intravenous urography and analysis of the blood show in many cases progressive hydronephrosis and some renal insufficiency.

The operation is performed only in cases in which there is some intolerable condition. The results in 48 cases reported justified the risk.

[COMPILERS' NOTE.—Coffey reviewed the development of his technic of uretero-intestinal anastomosis, a procedure that if ultimately perfected will do much to change the course of urologic surgery. The average high mortality of the operation has mitigated against its popularity. However, the application of the method by its author, C. H. Mayo and others has been attended by results that show that the operation has passed the experimental stage and is at present adaptable to a considerable group of cases.]

The opportunity for total cystectomy and for resection of the prostate gland in cases of carcinoma could well be afforded by uretero-intestinal anastomosis. However, successful issues from such operative procedures are infrequently reported. We must as yet consider the Coffey operation in a stage of development, but what has been done with the method offers much of future promise.]

(To be Concluded)